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## ELECTROCONVULSIVE THERAPY IN TREATMENT-RESISTANT MANIA: CASE REPORTS

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Electroconvulsive therapy is known to be effective in the treatment of mood disorders, more specifically for depression and mania. Although a large body of evidence confirms the efficacy of electroconvulsive therapy in the treatment of mania, few prospective studies have been done to assess its effectiveness in treatment-resistant manic episodes. These case reports describe the initial results of a study that is being conducted to evaluate the efficacy of Electroconvulsive therapy among treatment-resistant bipolar patients.

**METHODS:** Three manic patients (according to DSM-IV criteria) who were considered treatment-resistant underwent a series of 12 bilateral Electroconvulsive therapy sessions. Before the treatment and then weekly, they were evaluated with the following rating scales: Young Mania Rating Scale, Hamilton Rating Scale for Depression, Brief Psychiatric Rating Scale, and Clinical Global Impressions—Bipolar Version.

**RESULTS:** The 3 patients showed a satisfactory response to Electroconvulsive therapy, although some differences in the course of response were observed.

**CONCLUSION:** These case reports suggest that Electroconvulsive therapy needs further evaluation for the treatment of resistant bipolar patients.

**DESCRIPTORS:** Bipolar mood disorder. Mania. Treatment. Drug resistance. Electroconvulsive therapy.

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For more than 60 years, since its introduction in the management of psychiatric disorders by Cerletti and Bini in 1938, Electroconvulsive therapy (ECT), although more frequently related to the management of resistant depression, has also been associated with the successful treatment of manic episodes. Actually, mania is considered the third most common indication for ECT in psychiatric practice<sup>1,2</sup>.

Mukherjee et al.<sup>3</sup>, in an excellent review, reported the response rates of ECT in the treatment of mania described by different studies between 1942 and 1992. The 15 studies reviewed included a total of 589 patients, 80% of them showing remission or marked clinical improvement.

Between 1942 and 1959, seven studies that included at least 20 patients each found a significant clinical improvement in 78% of the 400 manic patients evaluated<sup>3</sup>. In those studies, however, resistance to treatment was not a selection criterion, since the pharmacological approach to psychiatric disorders was in its infancy, and lithium was first introduced in the 1950s.

Another 6 studies using a retrospective design with a total of 150 patients were performed between 1976 and

1992. ECT-induced remission or clinically marked improvement was found in 85% of the 150 manic patients studied, but treatment resistance was not considered as a criterion for the patients' selection<sup>3</sup>. Some of these retrospective studies matched patients by sex and age and compared the response rates of manic patients treated with ECT (before the introduction of pharmacotherapy) and chlorpromazine; they concluded that ECT was an effective treatment, as compared to no treatment, including for those patients with no clinical response to chlorpromazine<sup>4,5</sup>. Thomas and Reddy<sup>6</sup> compared ECT, chlorpromazine, and lithium in the treatment of manic patients and could not find differences

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among the 3 groups. Alexander et al.<sup>7</sup> and Strömgen<sup>8</sup> studied the response to ECT among patients not responsive to pharmacotherapy (without specifying the criteria for treatment resistance) and found that 56% and 59% of the patients, respectively, showed a good response to ECT after failed pharmacotherapy.

Two prospective studies performed by Small et al.<sup>9</sup> and Mukherjee et al.<sup>10</sup>, which included a total of 39 patients, aimed at assessing the effectiveness of ECT for treating mania. Small et al.<sup>9</sup> compared the efficacy of lithium and ECT. The patients in the ECT group had not shown a satisfactory response to previous treatments, which were not described. Of the 17 patients referred for ECT, total or partial remission was observed in 100%, and the authors concluded that lithium and ECT were equivalent in their efficacy. Among patients with severe mania, however, ECT proved to be superior to lithium<sup>9</sup>. Mukerjee et al.<sup>11</sup> studied the efficacy of ECT and haloperidol plus lithium in manic patients who did not show a good previous response to neuroleptics or lithium. Remission was defined as when the patients did not meet criteria for mania or hypomania according to the Research Diagnostic Criteria (RDC)<sup>12</sup>. ECT was effective in 59% of 22 patients, but for some nonresponders, a worsening of the clinical picture was observed<sup>11</sup>. Of the 39 manic patients included in both studies, ECT was effective in 77%.

Schnur et al.<sup>13</sup> studied the response rates of ECT among treatment-resistant manic patients in a study that also aimed to identify possible predictive factors of nonresponse among these patients. The patients included in the study—selected using the criterion of treatment resistance—had been treated with lithium, (blood levels between 1.0 and 1.5 mEq/L), or neuroleptics (dosages equivalent to 1500 mg/day of chlorpromazine) for 3 weeks, without clinical response. They

underwent an average of 9 daily bilateral sessions of ECT. Sixty-six percent of the patients showed a good response to ECT. Among nonresponders, the authors<sup>13</sup> identified some clinical characteristics such as anger, irritability, and suspiciousness.

There are large differences among these studies. The diagnostic criteria adopted in the patients' selection and the methodology employed (for example, retrospective versus prospective designs, absence of a control group in some studies, and criteria of remission and clinical improvement) were different, but ECT was unequivocally associated with successful treatment of mania.

We present preliminary cases of a study designed to evaluate the efficacy of ECT in bipolar pharmacotherapy-resistant patients.

## METHODS

The patients were referred for ECT after being considered treatment-resistant according to the following criteria: (1) *Bipolar mood disorder (BP)*: manic, mixed or depressive episode, according to the Structured Clinical Interview Diagnostic—SCID (version 2.0, 8/98)<sup>14</sup> that follows the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> edition—DSM-IV<sup>15</sup>. (2) *Treatment-resistant mania*: manic episode not responsive to at least 2 anti-manic treatments (for example, 1 mood stabilizer and 1 neuroleptic or combinations of mood stabilizers) in adequate dosages for 6 weeks (blood levels of lithium between 0.8 and 1.2 mEq/L, carbamazepine between 8 and 12 µg/mL, valproic acid between 45 and 125 µg/mL, and neuroleptics in doses equivalent to 5-20 mg/day of haloperidol). An additional inclusion criterion was a Young Mania Rating Scale (YMRS) total greater than 16<sup>16</sup>. (3) *Treatment-resistant bipolar depression*: depressive episode not re-

sponsive to at least 2 trials with antidepressants for 8 weeks in adequate dosage regimens, in association with a mood stabilizer, also with adequate blood levels as described above for lithium, carbamazepine, and valproic acid. Antidepressant dosage regimens were considered adequate when they were equivalent to 60 mg/day or maximum tolerated dose of fluoxetine or 80 mg/day or maximum tolerated dose of tranylcypromine. As an additional criterion, a total score of 18 was required on the Hamilton Rating Scale for Depression (HAMD-21, 21 items)<sup>17</sup>.

After the informed consent was signed, routine laboratory tests (total blood cell count, serum electrolyte levels, urinalysis, glycemia, blood urea and creatinine, thyroid screening tests, chest x-ray, electroencephalogram, and a computed tomography (CT) scan of the brain), were performed. The patients also underwent cardiac, odontological, and neurological evaluations to identify possible clinical conditions that would counterindicate ECT. These are necessary procedures for every patient referred for ECT, according to the Biological Treatment Unit—ECT of the Institute of Psychiatry—HCFMUSP<sup>18</sup>. The current medication was withdrawn by 50% on the first day, and by 25% on the following days until total discontinuation.

After 1 week of washout, the patients underwent 12 sessions of bilateral ECT in a 3-times-a-week schedule under anesthesia with atropine (0.4 to 1.0 mg/kg) and etomidate (0.2 to 0.3 mg/kg, or in case of intolerance, propofol, 2 to 2.5 mg/kg) and muscle relaxation with suxamethonium chloride (0.6 mg/kg). The ECT device used in the study was a Thymatron (TM) DGx, which offers a brief-pulse square wave delivered with a constant current of 0.9 A. The electrically induced seizure was considered adequate when its duration was greater than 20 seconds.

Before and after the washout week, as well as weekly during the 12 ECT sessions (after the 3<sup>rd</sup>, 6<sup>th</sup>, 9<sup>th</sup> and 12<sup>th</sup> session), the patients were evaluated with the following scales: YMRS<sup>16</sup>, HAMD-21<sup>17</sup>, Brief Psychiatric Rating Scale (BPRS)<sup>19</sup>, and Clinical Global Impressions—Bipolar Version (CGI-BP)<sup>20</sup>.

Clinical response was considered to be at least a 50% reduction in the YMRS and HAMD-21 scores, with final scores of the YMRS lower than 12 and HAMD-21 lower than 8.

**RESULTS**

**Case Nº 1**

Male, 29 years old, separated, 2 daughters. Family history of generalized anxiety disorder and major depression (sister). First episode at age 21, with psychotic symptoms, when he was diagnosed as schizophrenic. During this episode, he received ECT with good response (number of treatments and electrode placement not available). At age 26, he was hospitalized again for 3 months and received neuroleptics (haloperidol and chlorpromazine, dosage regimens not available). The next year after his brother’s death, he developed a period of agitation, insomnia, and hyperactivity lasting 1½ months. Hospitalization was not necessary, since he improved with neuroleptic treatment. The third and fourth hospitalizations occurred because of episodes of extreme psychomotor agitation, insomnia, mystical and persecutory delusions, and auto- and hetero-aggressive behavior that lasted an average of 3 months. After the fourth hospitalization, he started maintenance treatment with haloperidol (average dose of 10 mg/day), and 1 year later had a mild episode of agitation and increased activity for 1 month. The fifth hospitalization 1 year later lasted 6 months be-

cause of a severe episode of 10 months duration. He showed the same characteristics described above, attempted suicide, and was diagnosed as bipolar, manic, with psychotic symptoms. Treatment with lithium was started, with blood levels maintained between 0.8 and 0.9 mEq/L. The first depressive episode broke up 8 months later, and after a week receiving sertraline 50 mg/day in association with lithium, he switched to mania. Haloperidol was then introduced at 15 mg/day after the interruption of the antidepressant; lithium was maintained at 1350 mg/day (blood level at 0.9 mg/day), and after 6 weeks, carbamazepine (600 mg/day) was introduced. After 10 weeks with no adequate response, he was referred for ECT.

According to the SCID, the diagnosis was current manic episode with mood-incongruent psychotic symptoms, and as additional conditions, past alcohol and cocaine abuse. Relatives reported that the patient always increased alcohol consumption and started cocaine abuse after the worsening of the affective symptoms. All laboratory tests cited above were within the normal range. Clinical and neurological evaluations did not show a pathological condition. The initial and subsequent scores

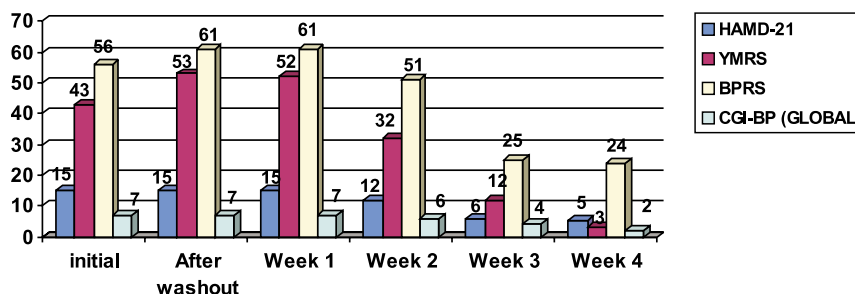
of the rating scales are described in figure 1. (Table 1).

**Case Nº 2**

Male, 50 years old, divorced, no children. Family history of bipolar disorder (BP) (sister confirmed, brother, father, and grandmother suspected) and alcohol and cocaine abuse (brother and uncle). First episode at age 30, with manic symptoms. History of 19 manic and 8 depressive episodes (shorter and milder than the manias) and 10 hospitalizations, all for mania. Comorbidity of AIDS, diagnosed 7 years previously. It is not clear whether his contamination was after a blood transfusion during a treatment for malaria or was a consequence of promiscuity coincident with a manic episode. During the first 6 years, he had a frequency of 1 manic episode every year. After 1987, however, when he first manifested depressive symptoms for 1 month, the frequency of the episodes increased, with an average of 2-3 per year. At that time, he was taking lithium (1500-2400 mg/day) with neuroleptics (haloperidol, 3-15 mg/day, or trifluoperazine, 5-15 mg/day) added as needed for the treatment of manic episodes, as well as antidepressants for depressive episodes (imi-

**Table 1** - Initial and subsequent total scores of the rating scales – Case Nº 1.

	initial	After washout	Week 1	Week 2	Week 3	Week 4
HAMD-21	15	15	15	12	6	5
YMRS	43	53	52	32	12	3
BPRS	56	61	61	51	25	24
CGI-BP (GLOBAL)	7	7	7	6	4	2



**Figure 1** - Initial and subsequent total scores of the rating scales – Case Nº 1.

pramine, 50-200 mg/day, when he switched to mania, and moclobemide, 200-400 mg/day). After a manic episode at the beginning of 1993, the maintenance treatment included lithium and neuroleptics. For almost 2 years, the patient remained relatively well, when a new hypomanic episode erupted at the end of 1994. During 1995, the patient remained in mania/hypomania for 9 months, with brief euthymic periods, and remained almost 8 months at the hospital. At that time, he had some clinical complications, such as 2 instances of possible lithium intoxication, worsening of the renal function, and diabetes insipidus. After many discontinuations, lithium was maintained at 600 mg/day (blood levels around 0.6 mEq/L), carbamazepine was added (reaching 1600 mg/day, blood levels 8-10 µg/mL), and neuroleptics were maintained (haloperidol, 2.5 to 7.5 mg/day; risperidone, 6 to 10 mg/day, in association at the beginning; risperidone on an average of 8 mg/day thereafter). The next year, he had only 2 questionable periods of hypomania and a mild depression for 1 month (citalopram was introduced at 20 mg/day and maintained for 4 months; neuroleptics were withdrawn). He developed diplopia as a side effect, and carbamazepine was reduced to 1000 mg/day, with resolution of the symptoms. Irritability remained a constant complaint and clinical symptom. At the beginning of 1997, he was again hypomanic. Valproate was introduced in substitution for carbamazepine, increased up to 2000 mg/day (blood levels, 59 µg/mL), lithium was increased up to 750 mg/day, and clonazepam was added up to 9 mg/day, but he remained irritable, more talkative, with questionable plans for almost the entire year. In November 1997, a new depressive episode was treated with citalopram, 20 mg/day, for 4 months, valproate was maintained at 2000 mg/day, and lithium was increased up to 1050 mg/day. He remained well for 6 months.

Routine laboratory evaluations revealed elevated TSH levels (5.3 mUI/mL), leading to levothyroxine replacement up to 50 µg/day. He developed a new manic episode in June 1998, when valproate was increased up to 3000 mg/day; risperidone, 4 mg/day, was added, but lithium had to be reduced to 600 mg/day because of the worsening of polyuria. He developed nausea and vomiting, and valproate had to be reduced to 1750 mg/day. A milder manic episode developed again and improved after the elevation of the risperidone (1 to 2 mg/day), and hypermetabolic administration of thyroxin was tried (150 µg/day). He remained well for 2 months, but again manic symptoms arose. Risperidone was increased to 4 mg/day; valproate was changed for lamotrigine, reaching 75 mg/day.

He was referred for ECT after a trial of lithium 600 mg/day (blood levels, 0.9 mEq/L), lamotrigine, 75 mg/day; risperidone, 4 mg/day; and clonazepam, 2 mg/day, without improvement of the manic symptoms for almost 8 weeks. Concurrent medication was indinavir, 2400 mg/day; stavudine, 80 mg/day; Epivir, 300 mg/day; and sodium levothyroxine, 150 µg/day, for

the management of lithium-induced hypothyroidism.

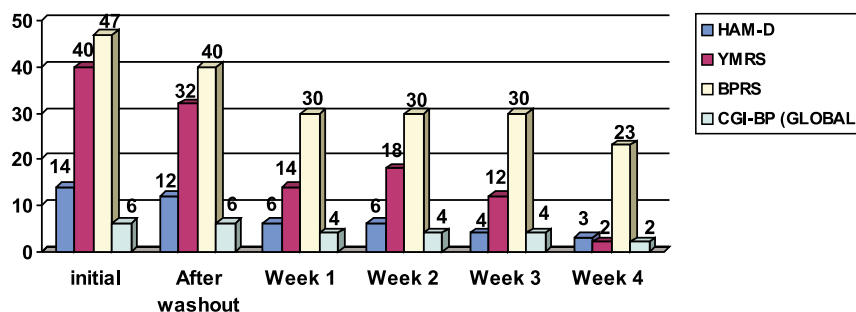
According to the SCID, the diagnosis was current manic episode without psychotic symptoms with comorbidity of AIDS and subclinical hypothyroidism. Laboratory tests were normal, including TSH, 1.2 mUI/mL; free T4, 1.5 mUI/mL; CD4, 419; and CD4/CD8, 0.31. No tomographic abnormalities were observed. The neurological and clinical evaluations were normal. Psychiatric medication was withdrawn at the rate described for case 1, and the anti-retroviral drugs and l-thyroxin were maintained during the series of ECT procedures. Occasionally, promethazine, 25 mg P.O., was administered because of insomnia. The initial and subsequent scores of the rating scales are described in figure 2. (Table 2).

**Case N° 3**

Female, 41 years old, divorced, 2 children. No family history of BP. First episode at age 26, in the 2<sup>nd</sup> puerperium, diagnosed as puerperal psychosis and treated with amitriptyline, 225 mg/day, and diazepam, 10 to 20 mg/day. She switched to mania and started taking lithium (900 to 1050 mg/day;

**Table 2 -** Initial and subsequent total scores of the rating scales – Case N° 2.

	initial	After washout	Week 1	Week 2	Week 3	Week 4
HAM-D	14	12	6	6	4	3
YMRS	40	32	14	18	12	2
BPRS	47	40	30	30	30	23
CGI-BP (GLOBAL)	6	6	4	4	4	2



**Figure 2 -** Initial and subsequent total scores of the rating scales – Case N° 2.

blood levels, 0.7 mEq/L) and haloperidol (15 mg/day). Two months later, she switched to depression. For 2 years she lived in another country, and relatives reported that she was treated with ECT and neuroleptics without mood stabilizers, probably because of another manic episode (no details regarding ECT and neuroleptic treatments could be obtained). Back in Brazil, she became depressed and started taking amitriptyline, 75 mg/day, for 1 month, switching to mania. A third hospitalization was needed because of the severity of the episode and the presence of psychotic symptoms. Chlorpromazine, 400 mg/day, was given for 1 month, and lithium was restored reaching 1200 mg/day (blood levels, 1.0 mEq/L). After 2 months of euthymia, a new depressive episode led to the introduction of tranylcypromine, 10-20 mg/day. TSH levels were increased (39.5 mUI/mL), and l-thyroxin, 150 µg/day, was added (TSH was 1.2 mUI/mL after 3 months). Almost 1 year later, a new mild and brief depressive episode was treated with fluoxetine, 20 mg/day, with the patient remitting in 1 month. The patient remained euthymic for the next 18 months, but she stopped taking medication in order to "lose weight". A new depressive episode occurred, and the patient switched again to mania after 1 month of lithium, 900 mg/day; tranylcypromine, 10 mg/day; and l-thyroxin, 150 µg/day. The fourth hospitalization lasted 2 months. She was then maintained on lithium, but thyroid supplementation was interrupted (reason not described). Five months later, she was hospitalized for 3 months in a psychotic manic episode. Subsequently, the first mixed episode was suspected. Lithium was maintained (1200 mg/day, blood levels between 0.8 and 1.0 mEq/L); risperidone, 2 mg/day (for 1 month), and clonazepam, 2 mg/day, were added. A new thyroid screening revealed increased TSH levels in May 1994, and therapy

with l-thyroxin was restored at 50 µg/day. Three months later, after taking the medication in an irregular way, a new manic episode with psychotic symptoms occurred. After being hospitalized for 2 months (lithium was maintained, carbamazepine was introduced and increased to 500 mg/day, and haloperidol was introduced and maintained for 2 months), she was discharged, but 1 month later needed to be hospitalized again in the second possible mixed episode. Carbamazepine was increased to 1000 mg/day and lithium to 1500 mg/day (blood levels, 1.2 mEq/L), and haloperidol was restarted at 5 mg/day. After 3 months, she left the hospital, but a possible mild mixed episode was monitored for 7 months. With the resolution of the symptoms, she remained well for almost 1 year, receiving lithium, 1350 mg/day (mean blood level, 0.8 mEq/L); carbamazepine, 1200 mg/day (mean blood level, 10 µg/mL); and l-thyroxin, 100 µg/day. A mild hypomanic episode developed, but the institution of clonazepam at 2 mg/day apparently stopped the symptoms. The next winter, she had a moderate depressive episode and took moclobemide for almost 9 months (3 months at 450 mg/day, 3 months at 900 mg/day, 2 months at 750 mg/day and 1 month at 300 mg/day). There was a suspicion of lithium toxicity, which led to the reduction of the lithium dose to 900 mg/day, which was increased to 1200 mg/day. Even with the reduction in the antidepressant dosage she had a mild switch to mania. Three months later, she was again hospitalized in a more characteristic mixed episode, when carbamazepine was discontinued, and valproate was introduced and increased to 2000 mg/day (blood levels, 100 µg/mL). Since she also developed psychotic symptoms, risperidone was added (4 mg/day, then reduced to 2 mg/day). During the mixed episode, l-thyroxin was increased to 150 µg/day.

Because of a suspected mild intoxication, lithium was reduced to 600 mg/day. One year later, with a maintenance treatment with valproate, 1000 mg/day (reduced because of the development of cutaneous rash); lithium, 750 mg/day; and l-thyroxin, 150 µg/day, she was mildly depressed. Tranylcypromine, 10 mg/day, was added. The patient again developed a mixed episode with psychotic symptoms and was then hospitalized for the ninth time.

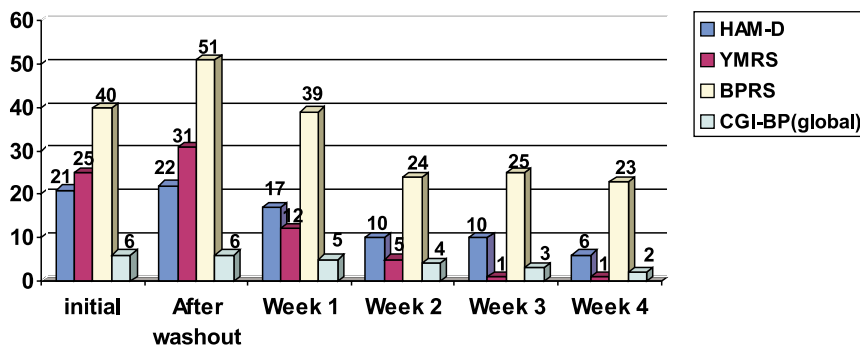
According to the SCID, the diagnosis was current mixed episode with psychotic symptoms with comorbidity of asthma, obesity, and subclinical hypothyroidism. When she was referred for ECT, she was on lithium, 1200 mg/day (blood levels, 0.7 mEq/L with 900 mg/day); valproate, 2000 mg/day (blood levels, 49 µg/day with 1000 mg/day); risperidone, 4 mg/day; and l-thyroxin, 150 µg/day. Lithium and valproate were discontinued, and since she remained agitated and the psychotic symptoms increased after the washout period, risperidone was maintained at 2 mg/day until the 5<sup>th</sup> administration of ECT. The initial and subsequent scores on the rating scales are described in figure 3. (Table 3).

## DISCUSSION

The initial HAMD-21 scores rated in case 1 represented the items insomnia, agitation, paranoid symptoms, and insight, which are actually manic symptoms. After the washout period, there had been a worsening of the clinical picture as was also evidenced by the rating scales. Concurrent medication was needed because of the extreme psychomotor agitation, aggressive behavior, and risks for the patient (self-injury, injury of other patients). During the weeks 1, 2, and 3, he received an average of 10 mg haloperidol/day I.M. and short half-life benzodiazepine (midazolam 15 mg P.O.) for

**Table 3** - Initial and subsequent total scores of the rating scales – Case Nº 3.

	initial	After washout	Week 1	Week 2	Week 3	Week 4
HAM-D	21	22	17	10	10	6
YMRS	25	31	12	5	1	1
BPRS	40	51	39	24	25	23
CGI-BP(global)	6	6	5	4	3	2



**Figure 3** - Initial and subsequent total scores of the rating scales – Case Nº 3.

insomnia as needed. After the 9<sup>th</sup> ECT session, he showed improvement according to the clinical evaluations and rating scales, and the medication was discontinued. After 12 ECT sessions (all effective), he remitted. Mild headache was the only reported side effect mainly after the ECT sessions, and these always remitted with dipyrone, 30 gtt P.O.

Some authors<sup>9,13</sup> report that a significant clinical response of manic episodes may be evident only after the 9<sup>th</sup> administration of bilateral ECT. Schnur et al.<sup>13</sup> suggested that the presence of symptoms like suspiciousness, irritability, and anger might contribute to a poorer response to ECT. The rapid withdrawal of lithium may also have contributed to the worsening of the manic symptoms after the washout week<sup>21</sup>. A particular difficulty observed in the management of the patient was the maintenance of a 3-times-a-week schedule, sometimes because of national holidays (when the ECT unit is closed), and other times because it was difficult to sustain the fasting as requested. This reinforces the importance of keeping a rigorous schedule for these patients.

In case 2, the HAMD-21 scores related to insomnia, agitation, psychic and somatic anxiety, and insight, which also related to the manic symptoms, as in case 1. In this case, it is noteworthy that after the washout period, a reduction in the scores was observed. One reason could be that AIDS patients (and more frequently those with AIDS dementia) are more sensitive to polypharmacy, especially to side effects, and prone to develop delirium with psychomotor agitation and behavioral changes<sup>22,23</sup>. Treisman et al.<sup>23</sup> suggested that the use of lithium in AIDS patients could be complicated because of the high rates of associated delirium and toxicity, and because of fluctuation of blood levels. This possibility could be speculated for this case, although no impairment of consciousness was observed, and the electroencephalogram, computer tomography, and neurological evaluation did not show a pathological condition at admission. However, normal CT images can be obtained in the initial stages of AIDS dementia<sup>22</sup>. Although lamotrigine has been successfully used in AIDS patients, there are reports of some mood elevating properties, and this should be

taken into account in this case<sup>23</sup>. After the initial reduction, an elevation of YMRS scores was observed. This elevation could be explained by the prolonged interval between weeks 1 and 2, and even by the patient's associated clinical condition (he developed a urinary infection and fever, which contributed to the cancellation of one ECT session). There might also have been a worsening of the manic episode during the ECT course as described by Mukherjee et al.<sup>10</sup> and Schnur et al.<sup>13</sup>. As also seen in case 1, the response was more evident after the 9<sup>th</sup> ECT; after the 12<sup>th</sup> ECT, the patient was considered remitted according to the clinical evaluation and the rating scales. In the literature, there are also reports of successful treatments of depressive episodes and stupor among serum-positive and AIDS patients with ECT<sup>24,25</sup>. Moderate headache and nausea were frequently reported after the ECT sessions, but stopped after treatment with dipyrone, 30 gtt P.O. Memory impairment was the most important complaint during the 3 weeks that followed the ECT course, but it later improved.

Differently from the others discussed above, the HAMD-21 items scored in case 3 represented symptoms such as depressive mood, guilt feelings, agitation, psychic and somatic anxiety, mood variation, and paranoid symptoms. There are no controlled studies designed to assess the efficacy of ECT in mixed states. Case reports and naturalistic studies suggest that ECT is a good treatment option for these patients, who are less responsive to lithium, but who show an adequate response to anticonvulsants, especially to valproate<sup>26</sup>. Dilsaver et al.<sup>27</sup> reported recovery among 7 patients with depressive mania treated with ECT. The presence of depressive symptoms could explain the faster response to ECT, with a good clinical improvement observed after the 6<sup>th</sup> administration, as already described by other authors<sup>9,13</sup>.



Small et al.<sup>9</sup> reported indeed that the presence of depressive symptoms was the strongest predictor of good response to ECT. Even with the faster response and greater initial reduction in the YMRS total values, the depressive symptoms remained until the 12<sup>th</sup> ECT. The final HAMD-21 value was lower than 8, suggesting clinical remission, but the patient was still reporting diminished interest, guilt feelings, feelings of uselessness, and some degree of anxiety. After the discontinuation of the mood stabilizers and during the course of ECT, the eating binges diminished, so the patient could lose weight. This is important when considering the comorbidity with obesity and its related risks, and because the weight gain is associated with medication non-compliance in many cases<sup>28</sup>. Kawachi<sup>29</sup> also reported that along with the increased risk of developing type II diabetes, hypertension, and coronary heart

disease (increasing the risk of death), weight gain was also associated with a poorer quality of life and stigmatization. Headache and memory impairment were side effects related to ECT. The patient had already complained of headache before the initiation of the ECT course, and there was no worsening of the condition. The memory impairment clearly developed in relation to ECT and was rated as moderate.

### CONCLUSION

The 3 cases reported here have shown a good clinical response to ECT after treatment resistance defined according to the mentioned criteria. Although obviously not statistically significant, these case reports remind us that ECT might be useful in the management of treatment-resistant patients because of its effectiveness; it should

not be considered as a “last resort” in the treatment of bipolar patients.

Remaining questions are to consider whether ECT is associated with a better or faster response than the new pharmacological options such as the anticonvulsants (valproate, lamotrigine, gabapentin, and topiramate) and the atypical antipsychotics (risperidone, clozapine, olanzapine, and quetiapine). This is an important issue that deserves attention in the future, especially to consider the cost-benefit relationship of the treatment adopted. The faster, more accessible, and cheaper treatment may gain the advantage, principally in countries where the economic issues of the treatment of bipolar patients are important. Another important issue that needs to be addressed is the effectiveness and tolerability of continuation and maintenance of ECT among these patients.

### RESUMO

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SOARES MB de M e col. - A Eletroconvulsoterapia no tratamento da mania resistente: relatos de casos. **Rev. Hosp. Clín. Fac. Med. S. Paulo** 57(1):31-38, 2002.

A Eletroconvulsoterapia é uma alternativa reconhecidamente eficaz no tratamento dos transtornos do humor. Embora vários estudos tenham confirmado a eficácia desta modalidade terapêutica no tratamento da mania aguda, poucos estudos foram realizados em pacientes maníacos resistentes à farmacoterapia. Esses relatos de casos descrevem resultados preliminares de

um projeto de pesquisa que tem por objetivo avaliar a eficácia da Eletroconvulsoterapia no tratamento de transtornos bipolares resistentes.

**MÉTODOS:** Três pacientes com diagnóstico de mania (de acordo com os critérios do DSM-IV), considerados resistentes ao tratamento medicamentoso, foram submetidos a 12 aplicações bilaterais de Eletroconvulsoterapia. Antes do tratamento e semanalmente, até o final da série, foram avaliados com as escalas: Young Mania Rating Scale, Hamilton Rating Scale for Depression, Brief Psychiatric Rating Scale e Clinical Global Impressions-Bipolar Version.

**RESULTADOS:** Os três casos aqui relatados apresentaram resposta satisfatória à Eletroconvulsoterapia, e aspectos individuais são discutidos.

**CONCLUSÕES:** Os resultados iniciais sugerem que a eficácia da Eletroconvulsoterapia no tratamento de pacientes bipolares resistentes deve ser melhor estudada.

**DESCRITORES:** **Transtorno bipolar do humor. Mania. Tratamentos. Resistência à drogas. Eletroconvulsoterapia.**

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