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A LONG TERM CLINICAL DIAGNOSTIC-THERAPEUTIC EVALUATION OF 30 CASE REPORTS OF BIPOLAR SPECTRUM MIXED STATES

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SUMMARY

The aim of this study is to show how managing long term patients who are diagnosed as having bipolar disorder with an affective mixed states can cause them to achieve a high level of recovery from the illness and quality of life.

This study observed all consecutive new patients who were seen in a private psychiatry practice during the years 2008-2009-2010 who had a diagnosis within the mixed states sub-group (Irritable Cyclothymia, Mixed Disphoria and Agitated Depression)Thirty patients were selected who presented with a score of less than 40 on the Global Assessment Scale (GAS). They were reassessed by readministering the GAS scale after six months and after two years treatment. The final results demonstrate an improvement of the mood of the patients and their increasing quality of life.Almost all reached a value on the GAS scale of between 60 and 80 after six months, and between 90 and 100 scores after two years.

Key words: *bipolar spectrum disorders – mixed states – long time treatment*

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BACKGROUND

The aim of this study is to show how to manage long time patients with serious mixed states bipolar disorders by describing 30 cases reports, and demonstrating that they can achieve a high level of recovery from the illness and improvement in the quality of life.

It has been described in previous papers that the mood in a person who is euthymic is stable while in mood disorders, the mood "swings" between depression and euphoria/irritability and therefore in mood disorders there is "unstable mood". A depressive episode is in fact only one phase of a broader "bipolar spectrum of mood", in which instability of the mood is the main component. The dysphoric component of the mood (mixed states) is quite frequent within all the subtypes of the bipolar spectrum (approximatively 30%; Tavormina 2010), above described:

- Bipolar I;
- Bipolar II;
- Cyclothymia;
- Irritable Bowel Syndrome Cyclothymia (rapid cycling bipolarity);
- Mixed Dysphoria (depressive mixed state);
- Agitated depression;
- Cyclothymic temperament;
- Hyperthymic temperament;
- Depressive temperament;
- Brief recurrent depression (Tavormina 2007).

CLINICAL EVALUATION AND METHODS

The dysphoric component of the instable mood is present in Irritable Cyclothymia, in Mixed Disphoria and in Agitated Depression. The main symptoms present are the following:

- overlapping depressed mood and irritability;
- high internal and muscular tension;
- reduced ability to concentrate and mental over-activity;
- gastrointestinal disorders, headaches, and various somatisation symptoms;
- insomnia (mainly fragmentary sleep);
- substance abuse (alcohol and/ or drugs);
- comorbidity with anxiety disorders;
- disorders of appetite;
- suicidal ideation.

As has been previously stated, (Tavormina 2007, Tavormina 2011, Tavormina 2012), it is essential, when making a correct diagnosis of bipolar spectrum disorders, to investigate the patient's personal past history of illness, his full family history regarding mood disorders, to assess the characteristic temperament of the patient from the beginning of his history of mood disorder, to assess the chronic presence throughout life in these patients of some somatic symptoms (especially: colitis, gastritis and headache). The co-presence of various types of somatisation symptoms, as well as the abuse of substances, should suggest the possibility of a "mixed state" of the bipolar spectrum.

In this study all consecutive new patients who visited a private psychiatric outpatient during the years 2008-2009-2010 who had a diagnosis within the mixed states sub-group (Irritable Cyclothymia, Mixed Disphoria and Agitated Depression), selecting (30 patients: 4 men, 26 women) those who presented with a score of less then 40 on the Global Assessment Scale (GAS). Then I assessed them again by administering the

Table 1. The improvement of the mood of the patients and medication in 30 patients

PT.	In.	6m.	Therapy	2y.	Therapy
1	30	50	Escitalopram (20mg) - Gabapentin (800mg) - Olanzapine (12.5mg) - Oxcarbazepine (150mg) - Paroxetine (30mg)	70	Escitalopram (20mg) - Gabapentin (800mg) - Olanzapine (2.5mg) - Carbamazepine (400mg) - Venlafaxine (75mg)
2	40	70	Sertraline (150) - Gabapentin (800mg) - Oxcarbazepine (450mg)	100	Sertraline (150) - Gabapentin (600mg) - Oxcarbazepine (450mg)
3	30	60	Sertraline (200mg) - Gabapentin (600mg) - Oxcarbazepine (600mg) - Olanzapine (7.5mg)	100	Venlafaxine (37.5mg) - Gabapentin (400mg) - Oxcarbazepine (600mg) - Aripiprazole (15mg)
4	35	80	Escitalopram (30mg) - Gabapentin (600mg) - Oxcarbazepine (150mg)	100	Escitalopram (10mg) - Gabapentin (300mg) - Oxcarbazepine (150mg)
5	35	70	Citalopram (40mg) - Duloxetine (60mg) - Carbamazepine (400mg) - Gabapentin (800mg)	90	Duloxetine (60mg) - Topiramate (75mg)
6	30	60	Venlafaxine (75mg) - Bupropione (150mg) - Gabapentin (1200mg) - Olanzapine (5mg)	90	Venlafaxine (37.5mg) - Bupropione (150mg) - Gabapentin (1200mg) - Olanzapine (7.5mg)
7	30	70	Venlafaxine (75mg) - Paroxetine (50mg) - Gabapentin (300mg) - Oxcarbazepine (900mg)	95	Paroxetine (20mg) - Gabapentin (400mg) - Oxcarbazepine (900mg)
8	35	65	Venlafaxine (225mg) - Gabapentin (1600mg) - Carbamazepine (300mg) - Trimipramine (25mg)	95	Venlafaxine (37.5mg) - Gabapentin (1200mg) - Carbamazepine (400mg) - Trimipramine (25mg)
9	30	55	Sertraline (75mg) - Gabapentin (800mg) - Valproate (500mg) - Oxcarbazepine (600mg) - Trimipramine (10mg)	90	Escitalopram (10mg) - Gabapentin (800mg) . Valproate (500mg) - Carbamazepine (400mg) - Pipamperone (20mg)
10	35	70	Bupropione (150mg) - Sertraline (100mg) - Valproate (500mg) - Amisulpride (300mg)	90	Bupropione (150mg) - Sertraline (50mg) - Valproate (500mg) - Amisulpride (200mg)
11	40	80	Sertraline (50mg) - Gabapentin (700mg)	100	Sertraline (25mg) - Gabapentin (300mg)
12	35	75	Sertraline (150mg) - Gabapentin (600mg) - Oxcarbazepine (600mg)	100	Sertraline (25mg) - Gabapentin (400mg) - Topiramato (75mg)
13	35	80	Paroxetine (30mg) - Gabapentin (400mg) - Oxcarbazepine (450mg)	100	Sertraline (50mg) - Gabapentin (300mg) - Oxcarbazepine (300mg)
14	35	85	Paroxetine (5mg) - Carbamazepine (400mg) - Gabapentin (400mg)	100	Carbamazepine (400mg) - Gabapentin (400mg)
15	30	55	Escitalopram (40mg) - Gabapentin (1600mg) - Valproate (1250mg) - Trimipramine (100mg) - Pipamperone (80mg)	95	Escitalopram (20mg) - Paroxetine (20mg) - Gabapentin (1200mg) - Oxcarbazepine (900mg) - Trimipramine (50mg) - Pipamperone (80mg)
16	30	70	Escitalopram (40mg) - Gabapentin (1200mg) - Carbamazepine (600mg) - Valproate (1250mg)	100	Escitalopram (10mg) - Gabapentin (800mg) - Valproate (1000mg)
17	35	75	Escitalopram (40mg) - Gabapentin (1200mg) - Oxcarbazepina (450mg)	100	Escitalopram (10mg) - Gabapentin (400mg) - Oxcarbazepine (300mg)
18	40	80	Paroxetine (20mg) - Gabapentin (800mg) - Carbamazepine (200mg)	100	Paroxetine (20mg) - Gabapentin (800mg) - Oxcarbazepine (150mg)
19	30	60	Venlafaxine (75mg) - Paroxetine (20mg) - Gabapentin (1600mg) - Valproate (1500mg) - Lithium (150mg) - Lamotrigine (50mg) - Olanzapine (15mg)	90	Venlafaxine (75mg) - Gabapentin (2000mg) - Valproate (300mg) - Lithium (150mg) - Lamotrigine (50mg) - Olanzapine (10mg)
20	30	65	Venlafaxine (300mg) - Paroxetine (40mg) - Gabapentin (1200mg) - Valproate (750mg) - Oxcarbazepine (450mg)	100	Venlafaxine (225mg) - Sertraline (50mg) - Gabapentin (1600mg) - Oxcarbazepine (600mg)
21	40	75	Escitalopram (10mg) - Gabapentin (500mg) - Oxcarbazepine (450mg)	100	Escitalopram (5mg) - Gabapentin (600mg) - Oxcarbazepine (450mg)
22	35	75	Sertraline (100mg) - Gabapentin (800mg) - Valproate (500mg)	100	Sertraline (25mg) - Gabapentin (800mg) - Valproate (250mg)
23	40	75	Escitalopram (10mg) - Gabapentin (1200mg)	100	Escitalopram (10mg) - Gabapentin (1200mg) - Oxcarbazepine (450mg)
24	30	75	Escitalopram (5mg) - Venlafaxine (37.5mg) - Gabapentin (1600mg) - Valproate (750mg) - Olanzapine (7.5mg)	95	Escitalopram (15mg) - Gabapentin (1200mg) - Valproate (1000mg) - Olanzapine (5mg)
25	35	80	Paroxetine (40mg) - Venlafaxine (37.5mg) - Valproate (500mg) - Gabapentin (600mg)	100	Venlafaxine (37.5mg) - Valproate (500mg) - Gabapentin (400mg)
26	30	75	Sertraline (25mg) - Gabapentin (1600mg) - Valproate (1250mg) - Oxcarbazepina (300mg)	90	Sertraline (25mg) - Gabapentin (1600mg) - Valproate (1000mg) - Oxcarbazepine (1200mg)
27	40	75	Escitalopram (10mg) - Gabapentin (1600mg) - Valproate (750mg)	95	Escitalopram (5mg) - Gabapentin (700mg) - Valproate (250mg)
28	35	60	Paroxetine (30mg) - Gabapentin (1600mg) - Valproate (750)	95	Escitalopram (5mg) - Gabapentin (1600mg) - Valproate (750) - Carbamazepine (800mg)
29	35	80	Escitalopram (5mg) - Gabapentin (1200mg) - Valproate (300mg) - Oxcarbazepine (600mg)	95	Escitalopram (10mg) - Gabapentin (1200mg) - Oxcarbazepine (600mg)
30	30	65	Escitalopram (10mg) - Gabapentin (1200mg) - Valproate (750mg) - Carbamazepine (100mg)	100	Escitalopram (5mg) - Bupropione (75mg) - Gabapentin (700mg) - Olanzapine (2.5mg)

Legend: PT. - ; In. - GAS data – initial; 6m. - GAS data - 6 months; 2y. - GAS data - 2 years

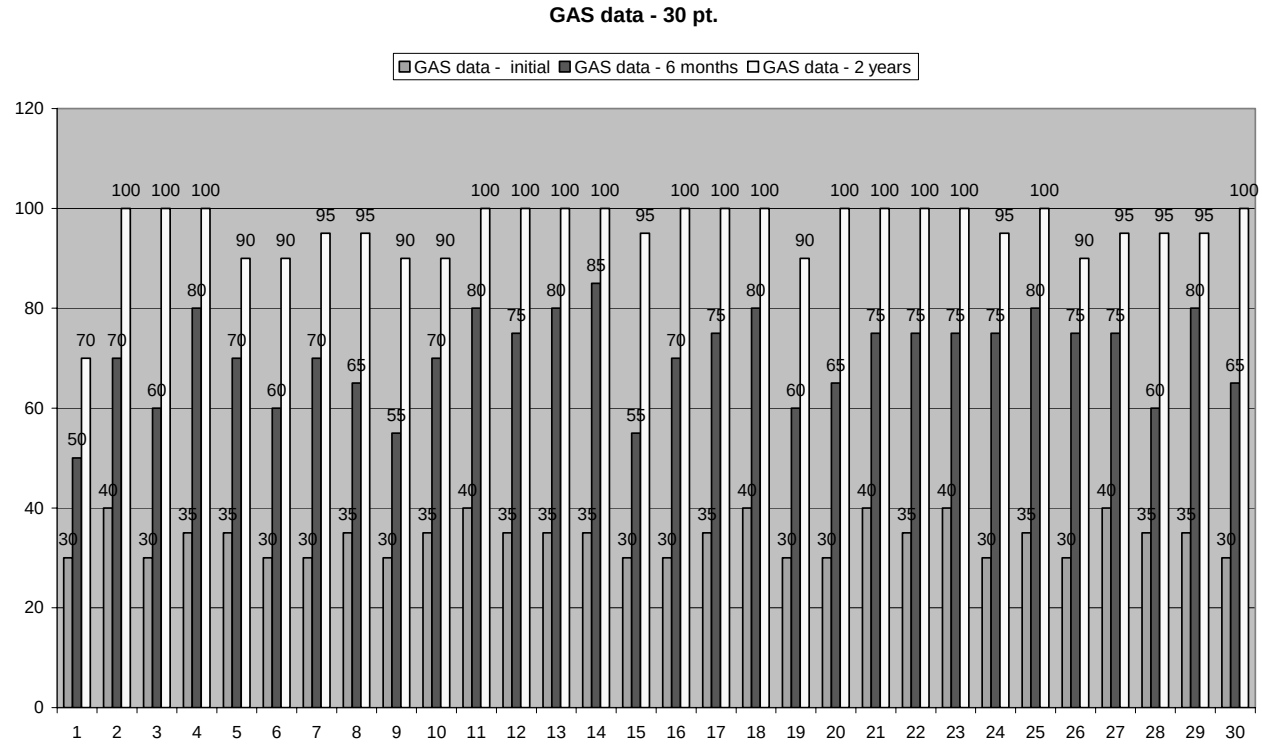

Figure 1. GAS Data 30 patients

GAS scale after six months and after two years of treatment.

The usual work in this clinic is to manage the mental health status of the patients over a long time, with periodical control-visits (every three weeks, monthly or every two months, as required).

RESULTS

The table 1 and the figure 1 depict the improvement of the mood of the patients and their improving quality of life (almost all reached a value at GAS between 60 and 80 after six months, and between 90 and 100 scores after two years).

The table summarises all patients data with the combination therapies used after six month and after two years.

The pharmacological therapy of mixed affective states consists of a polytherapy with mood-stabilisers (mainly: lithium, carbamazepine, valproate, gabapentin, oxcarbazepine, lamotrigine, topiramate, olanzapine, pipamperone) and antidepressants (mainly: SSRIs, SNRIs; and sometimes Bupropione. The clinician should never use antidepressants alone without mood-stabilisers when treating mixed states, in order to avoid an increase in dysphoria (Tavormina 2010, Agius 2011).

A correct maintenance therapy, however, assessed and chosen from case to case, based on the clinical picture should always include at least one or two mood stabilisers together with low doses of antidepressant (above all in maintainance therapy).

Gabapentin has been the most used mood-stabiliser in these patients in this study, for its tolerability and its effectiveness in combination with other drugs, in reducting of internal and muscular tension and improving colitis; above all, the utilization of Gabapentin in combination therapy allows a reduction in the dosages of Valproate and Carbamazepine/Oxcarbazepine and in consequence of this reduces their side effects (mainly: sedation, diplopia, amnesia, haematic and liver side effects, tremor, hair fragility).

Rarely we can obtain good results in stabilising bipolar disorders using only one mood-stabiliser, above all during the first period of treatment (one-two years).Very often one needs to use at least two or three mood-stabilisers in combination therapy.

CONCLUDING REMARKS

Long term management of affective mixed states gives the patients a high level of recovery from bipolar symptoms and improved quality of life. The patients need frequent follow up managing and modifing their drug therapy monthly if it is necessary.

The frequent necessity of the patient to resort to the use of benzodiazepines therefore becomes a tangible sign of clinical deterioration, which should prompt the patient and the psychiatrist to consider the need for adjusting the dosage of maintenance therapy.

The consequences of the lack of recognition and treatment of a mood disorder can instead lead to a higher risk of suicide, reduction in the expectation and/or the quality of life (personal, family and work), increased loss of working days, increased use of health

care resources, including for concurrent diseases. If unrecognised, the mood may become chronic and the clinical picture can worsen.

The following sentence of Hagop Akiskal is totally clear to show how important the work of the clinician is in these cases: "… The clinician involved in long-term care of bipolar spectrum patients is often the only stable anchor for them and, therefore, can be considered an interpersonal mood regulator …" (H. Akiskal - Bipolar Psychopharmacotherapy: Caring for the patient - 2005).

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