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Assessment of Olanzapine in Combined and Mono-therapy for the Treatment of Bipolar Disorder

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Abstract: In this report, collected data indicate the positive effect of olanzapine with high safety of margin. Combined therapy of olanzapine in the treatment of different subtype of bipolar disorder has a considerable benefit. It is appear that there is an agreement about olanzapine as a drug of choice in treatment of bipolar disorder. Consequently, further clinical studies are required with large number of population.

Key words: Olanzapine, bipolar disorder, monotherapy

INTRODUCTION

Bipolar disorder is a chronic mental illness characterized by multiple episodes (from one to several episode per day) of mania and depression. Bipolar disorder is often harder to treat than pure mania or unipolar disorders. After long time of neglect, some promising results have been accumulated during the last five years^[1]. Patients with bipolar disorder are more likely to seek medical counseling for depression than for mania. This is in part, due to depression affect the quality of life than does mania. The illness reflecting swings between mania and depression. Table 1 summarizes the clinical manifestations for bipolar disorder phases.

In fact, the depressive phase is associates with the substantial morbidity and mortality of the illness^[2]. A major advance in the treatment of this disorder has been achieved by the recognition of evidence for its subtypes^[3]. This helps the psychiatrists to predict the response to therapy and to initiate the right treatment regimens.

Bowden^[4] has divided bipolar to subtypes as mixed mania, secondary mania and mania associated with substance abuse and rapid cycling. The classification was based on the response to treatment with valproate, lithium, lamotrigine, carbamazepine or olanzapine. In brief,

mixed mania or depressive mania occurs with patients having depressive or irritable symptomatology. These patients response to valproate more than lithium or carbamazepine. Rapid cycling occurs in 15% of patients with poor response to treatment with lithium or carbamazepine. Some patients response to valproate or lamotrigine in monotherapy. Combined therapy of lamotrigine with olanzapine is often needed for control of rapid cycling. Secondary mania present as a mixture of mania and prominent irritability. Lithium has limited benefit in this case while valproate either in monotherapy or in combination with other drugs has a good profile of success^[5].

Combined versus monotherapy drug regimens: In 1960's, bipolar-related mania was treated by antipsychotic like chlorpromazine and haloperidol; while until mid 1970's the psychiatric used for the first time the antimonic drug, lithium^[6]. In addition, the anticonvulsant drugs like carbamazepine and valproate have been also used. In early 1990's, atypical antipsychotic dugs were introduce as off-label drugs for treatment of bipolar disorder. This manuscript will discuss the use of olanzapine either alone or in combination with other medications. Olanzapine has been selected among other compounds because it withdraws the attention as a broad treatment for bipolar disorder^[6,7].

Table 1: Comparison between manic and depressive phases in bipolar disorder

Manic phase symptoms	Depressive phase symptoms
Feeling of increase energy	Low mood, sadness and can not concentrate
Often embroiled in sexual or financial indiscretion	Preoccupation with gloomy thoughts, death and disaster
In sight may be lost	Lost of social interest and motivation
There are displays of self esteem, ambitiousness and grandiose behaviour	Persistence worrying out of proportion to the causes and thought of suicide
Can be irritable, hostile, aggressive, grandiose tined with sadness	Sleep, appetite and sexual disturbance
Mild hypomanic with difficult to distinguish from "high spirits"	Psychomotor retardation, agitation and felt of worthlessness

Table 2: Studies on olanzapine that accumulated during last five years

Reference	Combined drug	Compared drug	Study interest	Main result(s)
Tohen <i>et al.</i> ^[9]		Haloperidol	Depression and cognitive symptoms	Olanzapine superior on haloperidol
Namjoshi <i>et al.</i> ^[7]	Lithium or valproate		Life assessment	Adjunctive treatment more significantly improve clinical and quality of life
Sanger <i>et al.</i> ^[12]		Placebo	Preventing rapid cycling bipolar	Olanzapine significantly superior to placebo
Sanger <i>et al.</i> ^[13]		Placebo	Acute mania	Olanzapine significantly superior to placebo
Tohen <i>et al.</i> ^[14]	Lithium or valproate		Prevention of recurrence of bipolar disorder	Combined therapy was more effective than lithium or valproate monotherapy
Yurgelun-Todd <i>et al.</i> ^[15]		Valproate	Acute mania	Olanzapine was superior to valproate
Tohen <i>et al.</i> ^[16]	Lithium or valproate		Remission	Combined therapy was more effective than lithium or valproate monotherapy
Tohen <i>et al.</i> ^[17]	Valproate		Bipolar mania	Olanzapine was superior to valproate
Gregor <i>et al.</i> ^[18]	Haloperidol		Improvement of social Schizophrenia	Olanzapine was superior to haloperidol
Rasmussen and Seager ^[19]	Fluoxetine		Bipolar depression	Combined therapy more effective than monotherapy
Donoghue ^[20]	Quetiapine or risperidone		Bipolar mania	Combined therapy more effective than monotherapy. Olanzapine alone has more side effect
Corya <i>et al.</i> ^[21]	Fluoxetine		Depressive disorder	Combined therapy showed rapid, robust, and sustained improvement with no increase in side effect
Vieta <i>et al.</i> ^[22]	Fluoxetine		Depressive disorder	As previous but different method of study
Kock <i>et al.</i> ^[23]	Fluoxetine		Acute mania	The combination has does not increase the risk of acute mania
Evans <i>et al.</i> ^[24]		Lithium	Prevention in bipolar disorder	Both compounds appear to be effective and safe in preventing relapse into mania
Brown <i>et al.</i> ^[25]		Risperidone	Improvement of bipolar severity	Olanzapine was superior to risperidone
Fellows <i>et al.</i> ^[26]		Risperidone	Cost effectiveness	Risperidone has lower costs for patient
David <i>et al.</i> ^[27]		Placebo or haloperidol	QTc interval	Olanzapine have a favourable QTc interval
Sutton <i>et al.</i> ^[28]		Risperidone	Efficacy in controlling psychosis in old patients	Olanzapine was superior in controlling negative symptoms
David <i>et al.</i> ^[29]		Placebo and lorazepam	Effectiveness and safety for acute bipolar mania	Olanzapine was rapidly-acting, effective and safe
Shi <i>et al.</i> ^[30,31]		Haloperidol	Clinical and work status outcome with bipolar disorder	Olanzapine was superior in improvement of clinical and work outcome
Esel <i>et al.</i> ^[32]		Placebo	Tardive dyskinesia in bipolar patients	Olanzapine decreases tardive dyskinesia
Frazier <i>et al.</i> ^[33]			Juvenile bipolar disorder	Olanzapine was an effective monotherapy for juvenile bipolar
Namjoshi <i>et al.</i> ^[34]	Lithium or valproate		Impact on clinical and humanistic outcomes in bipolar disorder	Olanzapine has a significant positive impact on bipolar patients
Masand <i>et al.</i> ^[35]		Risperidone	Concomitant need for lithium	Patients with olanzapine received higher dose than did those with risperidone
Tohen <i>et al.</i> ^[36]		Placebo	Effect in acute and long-term treatment of bipolar disorder with or without psychotic	No difference in antimanic response in the presence or absence of olanzapine
Tohen <i>et al.</i> ^[37]			Safety and QTc interval	There were no significant changes in QTc of olanzapine
Tohen <i>et al.</i> ^[38]		Placebo	Tolerance and adverse events in treatment of acute mania	Olanzapine was generally well tolerable
Frazier <i>et al.</i> ^[39]			Safety in juvenile bipolar disorder	No serious clinically significant safety concern to olanzapine
Namjoshi <i>et al.</i> ^[40]			Health related quality of life of bipolar disorder patients	Olanzapine positively and significantly impact several dimensions of health-related quality of life
Tohen <i>et al.</i> ^[41]	Fluoxetine		Treatment-resistant major depressive disorder	Combined therapy was superior efficacy compared to monotherapy of either drugs
Zhang <i>et al.</i> ^[42]		Haloperidol	Comparison in schizoaffective disorder bipolar type	Olanzapine appears to have mood stabilizing properties with reduction of manic symptoms
Zhang <i>et al.</i> ^[43]		Haloperidol	Assessment of cognitive function in schizoaffective type bipolar disorder	Olanzapine had an average reduction in schizoaffective bipolar type
Tohen <i>et al.</i> ^[44]		Placebo	Efficacy and safety in manic patients with and without psychotic feature	Results suggest that olanzapine is safe and effective in long term treatment of manic

Table 2: Continue

Reference	Combined drug	Compared drug	Study interest	Main result(s)
Tohen <i>et al.</i> ^[45]		Placebo	Efficacy and safety in acute manic patients	Olanzapine demonstrate superior efficacy and a favourable safety profile
Sanger <i>et al.</i> ^[46]		Placebo	Safety and effectiveness in rapid-cycling bipolar patients	Olanzapine was safe and effective in treating the manic symptoms in rapid-cycling bipolar patients

The combined drugs should have no pharmacokinetic interactions, nor additive effects. Case reports as well as open trials indicate that response to treatment is improved when more than one drug is used. Lithium-valproate regimen has shown to be more effective than monotherapy.

Olanzapine, atypical antipsychotic, plus lithium or valproate was superior to lithium or valproate plus placebo^[7].

Several studies have indicated the superior use of olanzapine alone or with other drugs in treatment of different subtypes of bipolar (Table 2). Tohen *et al.*^[8] indicated that olanzapine was superior to haloperidol with respect to thymoleptic effect in patient with manic and depressive subtypes. Moreover, the olanzapine plus fluoxetine combination has demonstrated efficacy for treatment-resistant depression^[9]. This research has shown that, in patients with bipolar associated mania, olanzapine has improve health-related quality of life than did haloperidol, but its effects were not statistically significant compared with valproate. According to recent study, olanzapine added to lithium or valproate has shown superior efficacy in improving bipolar depressed patients compared with lithium or valproate alone^[7]. From the discussion, it is may be conclude that combined therapy is more profound in treatment of bipolar than monotherapy. Large clinical data suggest that the atypical antipsychotic olanzapine may be more effective in acute and prophylactic treatment of some patients with bipolar disorder including patients resistant to treatment with mood stabilizers, electroconvulsive therapy and conventional antipsychotics^[10]. McElroy *et al.*^[11] have investigated the drug in term patients resistant to treatment. Table 1 abridges the different studies on the combined of other drugs with olanzapine.

It is obvious that olanzapine was a hub for substantial interest as a prototype in its class (Table 2). Combination therapy was more profound in treatment of some types of bipolar with minimal unwanted effects. This drug report may shed more light on these debatable strategies for the treatment of bipolar disorder.

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