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Mini Review

Quetiapine as the Pharmacological Treatment of Bipolar Depression

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Abstract

Treatment of bipolar depression is not achieved with conventional antidepressants. In recent years, certain antipsychotics have been used successfully, including quetiapine, which has gradually become the standard treatment.

Keywords: Bipolar depression; Antipsychotics; Quetiapine

Introduction

Bipolar depression confronts the clinician with a dual clinical and therapeutic problem. Clinical identification is still largely insufficient, too many bipolar depressions being characterized as unipolar. The presence of a (hypo-) manic or mixed episode is sometimes difficult to identify in the patient's "whole life" history because in the majority of bipolar disorders, depressive episodes largely predominate in intensity as well as in duration over manic episodes [1]. On the other hand, patients rarely identify their (hypo-) manic episodes as pathological and readily remember them as having been particularly good times in their lives. From this point of view, the gaze of those around you can be of great help in the diagnosis. Even if the diagnostic criteria for bipolar depression are the same as those defined for the major depressive episode of DSM, bipolar depression seems to present relatively specific clinical signs, and which should in any case attract the attention of the clinician. Importantly, the occurrence of suicidal risk is greater in bipolar depression than in unipolar depression, in an almost double ratio when comparing bipolar type II and unipolar [2]. Finally, it has been shown for a few years that classic antidepressants are difficult to use in bipolar depression or even deleterious [3].

The Different Therapeutic Strategies

The lack of consensus on the choice of treatment strategies for bipolar depression today represents one of the most critical difficulties for clinicians in the management of bipolar patients. Among the recent international recommendations, those of the BAP (British Association of Psychopharmacology) limit the choice of first-line treatment to only two strategies: quetiapine as monotherapy, or lamotrigine as monotherapy [4]. Other international recommendations propose as a first-line choice to use either "classic" strategies (e.g. lithium as monotherapy or in combination with an SSRI, combination lithium + divalproex), or innovative strategies (lamotrigine monotherapy, monotherapy quetiapine, or a combination of olanzapine + fluoxetine) [5]. The comparison of these different therapeutic strategies through a meta-analysis of 19 studies (Vieta et al. [6]) shows that, among all these therapeutic strategies, the best level of evidence for the curative treatment of bipolar depression is observed. with quetiapine monotherapy or with the combination of olanzapine + fluoxetine. Lithium, lamotrigine, aripiprazole and paroxetine did not differ significantly from placebo in terms of efficacy.

Mechanism of Action of Quetiapine

Quetiapine has a strong affinity for the serotonin 5HT1A and 5HT2A receptors and the dopamine D1 and D2 receptors [7]. This D2 dopaminergic antagonism acts on psychotic symptoms and helps control mood; it is combined with a high selectivity for 5HT2A receptors, the blocking of which promotes the release of dopamine in certain regions of the brain (prefrontal cortex and nigrostriatal pathway) ensuring better extra pyramidal tolerance than that of conventional neuroleptics and preservation of executive functions. Quetiapine also has a strong affinity for 5HT1A receptors, the activation of which appears to be responsible for beneficial effects on mood, anxiety and cognition [8]. There is also an affinity for histaminergic H1 (anxiolysis, sedation and increased appetite), as well as for alpha1-adrenergic receptors (dizziness, hypotension) and to a lesser extent for type 1 muscarinic receptors (dry mouth). In contrast, quetiapine has no affinity for cholinergic receptors. Norquetiapine, the active metabolite of quetiapine, appears to play an important role in the drug's efficacy profile. Indeed, in addition to the fact that norquetiapine has, like quetiapine, an affinity for the 5HT2 and D1 and D2 receptors, it has the particularity of exhibiting a strong affinity for the Norepinephrine Transporter (NET) [9]. This potent noradrenergic effect is likely to be involved in the particular efficacy profile of quetiapine on depressive symptoms in bipolar patients (Ki for norquetiapine: 12; for comparison, Ki for nortriptyline: 1.49-21; Ki for venlafaxine: 1060-6310; Ki for olanzapine:> 10,000 [10].

Efficacy Data for Quetiapine in Bipolar Depression

The efficacy of quetiapine in the treatment of depressive episodes associated with Bipolar I or II disorder has been established in several randomized controlled clinical trials. In a placebo-controlled trial with lithium (plasma serologies between 0.6 and 1.2 mEq / L.) Lasting 8 weeks (n = 802 bipolar I or II patients), patients took 300 mg or

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600 mg of quetiapine [11]. From the first week, quetiapine statistically significantly reduced symptoms of depression and this effect was maintained for the remainder of the 8 weeks of treatment. Lithium, on the other hand, was not significantly different from placebo. In the group taking quetiapine, 70% of patients were in remission at 8 weeks against 62% on lithium 56% on placebo. In four other 8-week clinical trials in bipolar depression quetiapine at doses of 300 and 600 mg / day, confirmed its efficacy on symptoms of depression, without benefit. additional 600 mg dose over 300 mg dose [12]. In a certain number of bipolar depressions which are difficult to treat, the question of therapeutic combinations frequently arises. Regarding the associations with quetiapine, the data are still too preliminary to draw any formal conclusions. As an exploratory study, a naturalistic study of 232 bipolar patients followed for four years, showed that dual lithium therapy quetiapine was more effective in preventing relapse than the combination lithium + valproate or than lithium, valproate monotherapies. or lamotrigine to prevent relapse [13].

Quetiapine monotherapy is effective for acute bipolar depression and the prevention of mania/hypomania switching [14].

Tolerance Data

Common side effects reported with quetiapine are, across all trials: dry mouth, drowsiness, sedation, weight gain (1.5 to 3 kg on average) and dyspepsia. In about 10% of patients, elevations in serum triglyceride and total cholesterol were observed (most often with increased LDL cholesterol and lower HDL cholesterol). In addition, 1 to 10% of patients presented with elevations in blood sugar. Very rare reports of QT prolongation have been observed with massive overdoses of quetiapine [15].

Conclusion

The particular psychopharmacological action profile of quetiapine and its active metabolite norquetiapine represents an advantage in the treatment of acute bipolar depression. Its safety profile highlights the risk of metabolic syndrome, a class effect of all atypical antipsychotics. Sedation and orthostatic hypotension are frequent at the start of treatment and justify gradual titration. Benefit-risk assessment and meta-analytical comparisons now place quetiapine compared to other mood stabilizers at the forefront of acute treatment for depression.

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