

Quetiapine Induced Cataract - A Rare Case Report

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Abstract Atypical antipsychotics are increasingly used as first-line treatment for bipolar disorder, in both acute mania and acute depression as well as in maintenance treatment. These have also been shown to be effective as add-on agents and in long term prophylaxis. The most common side effects are dry mouth, sedation, dyslipidemia, weight gain, constipation, altered blood glucose level and extra pyramidal side effects. Quetiapine induced cataract has been reported in animal studies and extrapolation on humans was described as rarity. Hence, the case is reported to highlight quetiapine induced cataract.

Keywords: bipolar disorder, Quetiapine, posterior capsular cataract, Montgomery Asberg Depression Rating Scale (MADRS), Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5), adverse event, Lens opacity classification system (LOCS)

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be aware of its side effects and six monthly regular eye check-up is recommended for assessment of cataract.

1. Introduction

Quetiapine is a dibenzothiazepine derivative that is a serotonin type 2 (5-HT_{2A}) and dopamine type 2 (D₂) receptor antagonist and it also interacts with other neurotransmitter receptors e.g., 5HT₇, 5HT_{2c}, α_1 and 2 antagonist, Histaminic (H₁) receptor antagonist, 5HT_{1A} partial antagonist etc... [1,2]. It is an orally administered atypical antipsychotic [3] that is indicated for the treatment of schizophrenia, manic episode in bipolar disorder [4] and bipolar depression [5,6] or as an adjunct to lithium or valproate semisodium; [7] and as maintenance treatment for bipolar disorder [8]. The antidepressant mechanism of action of quetiapine is uncertain, but may be related to its effects on 5-HT_{1A} and 5-HT_{2A} receptors in the prefrontal cortex, modulation of dopamine transmission and/or inhibition of synaptic noradrenaline reuptake as a result of the blocking of norepinephrine transporter (NET) by norquetiapine [9]. Quetiapine 300 mg per day or 600 mg per day is generally well tolerated and efficacious in patients with bipolar depression and the most treatment-emergent adverse events are mild to moderate in severity. The most frequent adverse events occurring during the acute treatment phase were dry mouth, sedation, dizziness, constipation and increased appetite [2]. There are various etiological factors of cataract e.g., senile, traumatic, metabolic, congenital and drug induced e.g., corticosteroids, miotics, amiodaron, statins, tamoxifen and phenothiazines [10]. Quetiapine has been found to be cataractogenic in dogs at high dosage i.e., 100 mg per kg or 4 times the maximum recommended human dose (MRHD) of 800 mg per day on mg/m² body surface area [1,11]. So, it is imperative for the clinicians to

2. The Case Report

A female aged 34 year, was a known case of bipolar II disorder and reported to out-door patient Department of Psychiatry, Government Medical College, Rajindra Hospital, Patiala with symptoms of sadness of mood, lassitude, hypersomnia, hyperphagia and psychomotor retardation for the last 3 months. The diagnosis was assessed by semi-structured clinical interview on Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) [12] that coded non-psychotic bipolar disorder as 296.89 bipolar II disorder, current episode depression with moderate severity. The severity of depression was assessed on Montgomery Asberg Depression Rating Scale (MADRS) [13] and clinical outcome on Clinical Global Impression-Severity (CGI-S) scales with scores of 30 and 4 respectively. She took quetiapine 50 mg per day that was gradually titrated to 300 mg per day on fourth day and continued thereafter for 14 months. She had achieved full remission from an episode of depression after 12 weeks with MADRS and Clinical Global Impression-Improvement (CGI-I) scales scores of 6, 2 respectively indicating much improvement. She continued treatment at the same therapeutic dose for 14 months to prevent further relapses and recurrences. After 9 months of treatment, she reported with complaints of diminution of vision, glare and poor vision under bright light for the last 5 months. These symptoms were gradual on onset, progressive and worsened in the evening. There were no other significant medical history e.g., diabetes, hypertension or intake of any substance/drug except that she was on antipsychotic

drug i.e., quetiapine 300 mg per day for the last 14 months. On local examination, her unaided visual acuity was 20/50 and 20/40 for right and left eye respectively. Her best corrected visual acuity was 20/20 for both eyes with refractive error of -1.0D Spherical/+0.5D Cylinder at 160 degree for right eye and +1.0D Spherical for left eye. Her intraocular pressure was 16 mm Hg and 14 mm Hg for right and left eye respectively. On slit-lamp examination, both eyes showed cataract and rest of anterior segment examinations were unremarkable. Corneas of both eyes were transparent without any deposits. After full dilatation of pupil, both eyes showed cortical cataract grade-3 with wedge shaped opacities (cortical spokes) at the periphery of the lens with pointed ends of opacities oriented towards the centre (Figure 2 a & b) and were seen as dark shadows on retro-illumination (Figure 3 a & b). In addition, right eye showed posterior subcapsular cataract of grade-3 according to Lens opacity classification system (LOCS-III). Fundus examination for both eyes was normal and her eyes examined before the start of therapy (Figure 1 a, b, c & d) and after every six months to rule out ocular toxicity. On WHO-UMC causality scale [20] it showed probable adverse drug reaction and Naranjo probability scale [21] score of 7 indicates probable association for quetiapine (administration of drug) induced cataract (a clinical event), of long duration (reasonable time sequence of more than 6 months) with no other confounding drug or diseases and rechallenge not required.

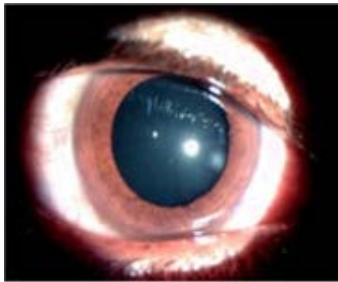


Figure 1 (a). Shows clear crystalline lens (right eye)

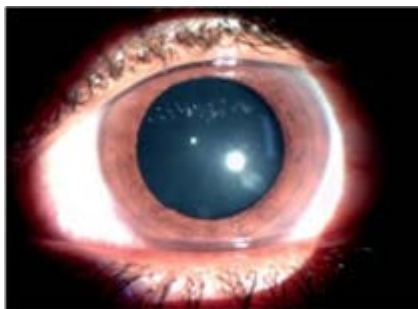


Figure 1 (b). Shows clear crystalline lens (left eye)

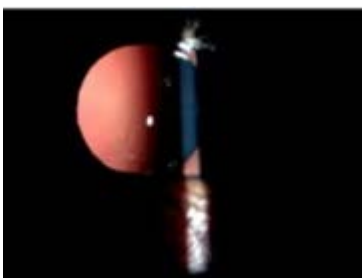


Figure 1 (c). Shows retro-illumination of right eye with no cataract changes

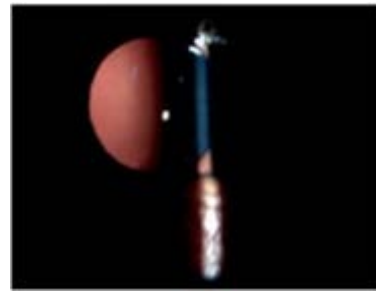


Figure 1 (d). Shows retro-illumination of left eye with no cataract changes



Figure 2 (a). Shows cortical cataract with peripheral spokes in right eye



Figure 2 (b). Shows cortical cataract with peripheral spokes in left eye

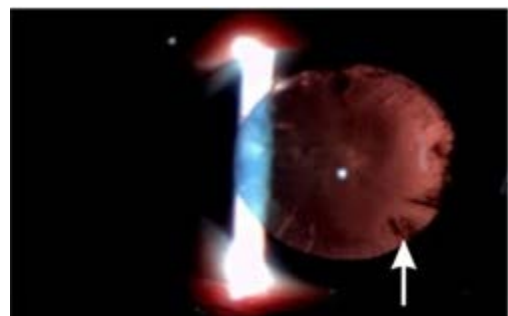


Figure 3 (a). Shows peripheral spokes and posterior subcapsular cataract on retro-illumination in right eye

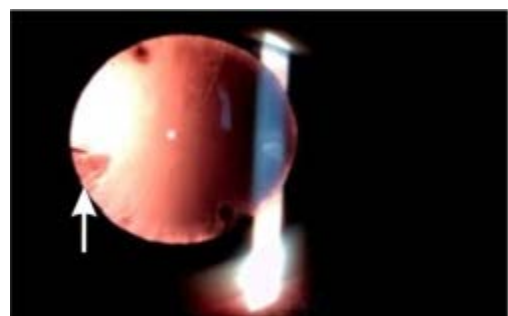


Figure 3 (b). Same on retro-illumination in left eye

3. Discussion

Bipolar depression is a common and debilitating disorder which differs from unipolar disorder in severity, time course, recurrence and response to the treatment. About 15 % of people with bipolar disorder commit suicide and bipolar depression entails a greater socio-economic burden than either mania or unipolar depression [14]. Quetiapine is efficacious in dose of 300- 600 mg daily (as monotherapy) in bipolar I and bipolar II depression, prevents relapse into depression and mania and is probably the drug of choice in bipolar depression [15]. Typical antipsychotic drugs, mainly phenothiazines, chlorpromazine and atypical antipsychotics e.g., olanzapine, risperidone and ziprasidone can lead to lenticular opacities [10]. There are anecdotal reports, about quetiapine showing ocular side effects e.g., cataract which are rare, transitory and infrequent [16]. The preclinical studies on dogs receiving quetiapine for 6 to 12 months showed focal triangular cataracts at the junction of posterior sutures in the outer cortex of lens. These findings may be due to inhibition of cholesterol biosynthesis by quetiapine. However, there was no correlation between plasma cholesterol and presence of cataracts in individual dogs [1]. The appearance of delta-8-cholesterol in plasma is consistent with inhibition at a later stage in cholesterol biosynthesis and there was 25% reduction in cholesterol content of the outer cortex of the lens [1]. The lipid lowering drugs e.g., simvastatin, pravastatin and lovastatin also interfere with cholesterol biosynthesis but showed no clear evidence about their cataractogenic potential [16]. In this case report, patient was on quetiapine dosage of 300 mg per day for the last 14 months. The above treatment was consistent with the Maudsley prescribing guidelines in psychiatry for long-term management of bipolar depression in continuation phase [15]. Valibhai et al., 2001 reported a case of lenticular changes after 15 months of quetiapine therapy for schizophrenia [17]. In this case, patient was of bipolar depression and required long term prophylaxis for management of current episode and prevention of further relapses and recurrences. Nasrallah et al., 1999 reported lens opacities in 15 patients taking quetiapine and majority of these patients had the following risk factors for cataract e.g., smoking, diabetes, hypertension, advanced age and pre-existing cataract [18]. However, in present case, patient was non-diabetic, non-hypertensive and non-smoker and unlikely to be cataractogenic. The one year study in female monkeys showed striated appearance of the anterior lens surface at a dose of 225 mg per kg or 5.5 times the MRHD of 800 mg per kg on mg/m^2 body surface area [1]. In this case, the types of lenticular changes in both eyes were peripheral cortical spokes and in right eye posterior subcapsular cataract of grade-3 according to (LOCS-III) which is at variance and indicate drug induced cataract. If the patient is on quetiapine, as reported in Stahl's prescriber's guide, 2009 [19] United States (US) manufacturer recommends six monthly eye check-up for cataract though unnecessary is at variance with our observation as highlighted in this case.

4. Conclusion

Patients on long-term atypical antipsychotic may develop metabolic side effects e.g., dyslipidemia, hypertension, weight gain, diabetes, obesity, extra-pyramidal side effects etc., and quetiapine is also not devoid of the above features but in addition to that there is higher preponderance of cataract formation that can be probable and unlikely to be attributable to another cause. Hence, patient on quetiapine should be assessed for ophthalmic examination at baseline and thereafter periodically at every six months.

5. Limitations of Study

The double-blind randomized, placebo controlled or prospective cohort studies are needed to generalize these intriguing findings and establish causality.

6. Implication/ Salient Features of this Study

Patients on atypical antipsychotic drug e.g., quetiapine when complaints of diminution of vision, glare or poor vision under bright light and no medical history of diabetes, hypertension, dyslipidemia etc., should be examined for drug induced ocular toxicity i.e., cataract.

7. Source of Support

Nil.

8. Conflict of Interest

None declared.

References

- [1] AstraZeneca Pharmaceuticals LP. Seroquel package insert. Wilmington, DE, AstraZeneca Pharmaceuticals, October, 2013 (http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=0584dda8-bc3c-48fe-1a90-79608f78e8a0#ID_1ead488d-26c6-4023-8222-129ac9cccf40). [Accessed on May 5, 2014].
- [2] Sanford, M. and Keating, G.M, Quetiapine a review of its use in the management of bipolar depression, *CNS Drugs*, 26:435-60.2012.
- [3] Kapur, S. and Seeman, P, Does fast dissociation from the dopamine D2 receptor explain the action of atypical antipsychotics? A new hypothesis, *Am J Psychiatry*, 158. 360-9. 2001.
- [4] Pharmacotherapy of psychosis and mania, In: Brunton LL, editor. Goodman and Gilman's *The pharmacological basis of therapeutics*. 11th ed. New York: McGraw- Hill, 2006, pp 461-500.
- [5] Calabrese, J.R., Keck, Jr, P.E., Macfadden, W. et al., A randomized, double- bind, placebo- controlled trial of quetiapine in the treatment of bipolar I or II depression, The BOLDER Study Group, *Am J Psychiatry*, 162. 1351-60. 2005.
- [6] Thase, M.E., Macfadden, W., Weisler, R.H. et al., Efficacy of quetiapine monotherapy in bipolar I and II depression: a double-bind, placebo- controlled study, The BOLDER II Study Group, *J Clin Psychopharmacol*, 26. 600-9. 2006.
- [7] Sachs, G., Chengappa, K.N., Suppes, T. et al., Quetiapine with lithium or divalproex for the treatment of bipolar mania: a randomized, double-blind placebo-controlled study, *Bipolar Disord*, 6. 213-23. 2004.
- [8] Thase, M.E, Quetiapine monotherapy for bipolar depression, *Neuropsychiatric Dis Treat*, 4. 11-21. 2008.

- [9] Jensen, N.H., Rodriguiz, R.M., Caron, M.G. et al., N-desalkylquetiapine, a potent norepinephrine reuptake inhibitor and partial 5HT_{1A} agonist, as a putative mediator of quetiapine's antidepressant activity, *Neuropsychopharmacol*, 33. 2303-12. 2008.
- [10] Fraunfelder, F.T. and Fraunfelder, F.W, *Drug induced ocular side effects*, 5th ed. Woburn: Butterworth-Heinemann, 2001, pp 824.
- [11] Sadock, B.J., Sadock, V.A. and Sussman, N, *Kaplan and Sadock's pocket handbook of psychiatric drug treatment*. 6th ed. Wolters Kluwer: Lippincott Williams and Wilkins, New Delhi, 2014, pp 229.
- [12] American Psychiatric Association, *Diagnostic and statistical manual of mental disorders*, 5th ed. American Psychiatric Association, Washington DC, 2013, pp 132-9.
- [13] Montgomery, S.A. and Asberg, M, A new depression scale designed to be sensitive to change, *Br J Psychiatry*, 134. 382-9. 1979.
- [14] Goodwin, G.M, Evidence- based guidelines for treating bipolar disorder: revised second edition- recommendations from the British Association for Psychopharmacology, *J Psychopharmacol*, 23. 346-88. 2009.
- [15] Taylor, D., Paton, C. and Kapur, S, Bipolar depression, In: *The Maudsley prescribing guidelines in psychiatry*, 11th ed. Wiley Blackwell, Great Britain, 2012, pp 185-91.
- [16] Stip, E. and Boisjoly, H, Quetiapine: are we overreacting in our concern about cataracts (the beagle effect)? *Can J Psychiatry*, 44. 503. 1999.
- [17] Valibhai, F., Phan, N.B., Still, D.J., True, J, Cataracts and quetiapine, *Am J Psychiatry*, 158. 966. 2001.
- [18] Nasrallah, H.A., Dev, V., Rak, I., Raniwalla, J, Safety update with quetiapine and lenticular examinations: experience with 300,000 patients. In: Abstracts of the 38th Annual Meeting of the American College of Neuropsychopharmacology, Nashville, Tenn, *Am Colleg Neuropsychopharmacol*, 1999.
- [19] Stahl, S.M, *Stahl's Essential Psychopharmacology, The Prescriber's Guide*, 3rd ed. Cambridge University Press, New Delhi, 2009, pp 460.
- [20] The use of the WHO-UMC system for standardized case causality assessment. Accessed at <http://www.who-umc.org/Graphics/24734.pdf> on June 18th, 2014.
- [21] Naranjo C.A., Busto U., Sellers E.M. et al., A method for estimating the probability of adverse drug reactions, *Clin Pharmacol Ther*, 30. 239-45. 1981.