Clozapine-induced maculopathy

In reply: We thank Mack and Symons for their comments on our article.[1] Our patient presented with bilateral asymmetric macular pigmentary changes, secondary to disturbances of the retinal pigment epithelium (RPE). Clinical examination findings corresponded with visual field and electrophysiology tests.

We acknowledge the dopamine hypothesis, but due to the constraints of the *MJA* snapshot format, this was not postulated or expanded on in our article. Clozapine is classified as a phenothiazine, which is a major class of antipsychotics with a well documented history of causing skin and ocular pigmentation.[2-4] Borodoker and colleagues[2] reported a case of long term thioridazine and chlorpromazine use associated with peripheral retinal hyperpigmentation and atrophic areas within the macula. Similarly, Lal and colleagues[3] reported an association between long term chlorpromazine therapy and pigmentation of the corneal endothelium and anterior lens capsule. On ceasing chlorpromazine, most patients experienced a decrease in ocular and accompanying skin pigmentation.[3]

There are two hypotheses for the pathogenesis of phenothiazine-induced ocular pigmentation, which may account for the ocular side effects of clozapine described in our patient. First, it is postulated that uptake of the drug occurs through the choroid, after which it binds to melanin in the RPE. This interrupts its ability to phagocytose rod photoreceptor outer segments,[4] which may induce pigmentary changes. Second, as the authors have noted, clozapine has a high affinity for dopaminergic D_1 and D_4 receptors,[5] the latter of which is highly expressed in the human retina.[4] The retinal dopaminergic system is integral to many aspects of retinal physiology, including melanin granule distribution within RPE cells and photoreceptor synthesis of melatonin. Blockade of retinal D_4 receptors by clozapine may increase melatonin production, which has been shown to induce photoreceptor damage on exposure to light.[4]

Therefore, we conclude that our findings of pigmentary changes on the corneal endothelium, lens capsule and macula were associated with clozapine use.

Jessica Y Tong[1]
Amy Pai[2]
Stephanie H Young[2]

1 Westmead Hospital, Sydney, NSW.
2 Concord Repatriation General Hospital, Sydney, NSW.

jton0648@uni.sydney.edu.au

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