Floppy iris syndrome with oral imipramine: A case series

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Intraoperative floppy iris syndrome (IFIS) has commonly been seen with long-term use of α1-adrenoceptor blocking agents. We observed IFIS in three patients during phacoemulsification due to oral imipramine therapy. The three patients took imipramine for 25 years, 10 months and 1 year, respectively. However, only the first patient was on oral therapy at the time of surgery, while the other two patients had stopped 4 months and 2 months prior to undergoing phacoemulsification. The first and third patients developed complete IFIS features, while the second had only partial IFIS characteristics. Phacoemulsification could be completed in all three patients without any complication. None of these patients had history of taking any of the α1-adrenoceptor

blocking agents. This is the first anecdotal report of IFIS with the oral use of imipramine and hence further evidences are required to ascertain the association of oral imipramine therapy and IFIS. However, ophthalmologists undertaking phacoemulsification on patients on imipramine therapy should be alert for the occurrence of IFIS.

Key words: Adrenergic blocker, imipramine, intraoperative floppy iris syndrome, iris hooks, phacoemulsification

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Intraoperative floppy iris syndrome (IFIS) during phacoemulsification has commonly been described in patients using long-term α1-adrenoceptor (AR)-blocking agents such as tamsulosin, doxazosin, alfuzosin, terazosin.[1] Recently, antidepressant and antipsychotic drugs like mianserin,[2] chlorpromazine,[3] and ropinirole[4] have also been reported to be associated with this syndrome. We hereby, report for the first time three patients who were on oral imipramine developed IFIS during phacoemulsification.

Case 1

A 65-year-old man with chronic depression and diabetes mellitus of 25 years and 15 years duration, respectively, presented to us with decrease in vision in both eyes. He was on insulin injections for diabetes mellitus and oral imipramine (25 mg twice daily) for depression over the previous 25 years. Anterior segment examination showed cataract in both eyes. Fundus examination showed mild non-proliferative diabetic retinopathy. He underwent phacoemulsification under local anesthesia. Preoperatively, the pupil dilated to 6.0 mm. During the phacoemulsification procedure, characteristics of IFIS developed: iris stroma was flaccid, which undulated, billowed, and prolapsed through the main and side incisions, and progressive miosis occurred. Intracameral adrenaline was injected, however the miosis and floppy iris did not improve appreciably. The phacoemulsification procedure was completed and intraocular lens was successfully implanted into the capsular bag.

Case 2

A 60-year-old man presented for painless progressive decrease in vision in both eyes. His ocular examination was normal other than the presence of cataract in both eyes. Preoperative evaluation was normal except poor mydriasis in both eyes. He gave a history of being on antidepressant, imipramine therapy (25 mg once daily) for 10 months, which he stopped 4 months prior to undergoing surgery. He was scheduled for phacoemulsification in the left eye under local anesthesia. Preoperatively, the pupil dilated to 5.0 mm. During the phacoemulsification procedure, partial IFIS characteristics developed i.e. progressive miosis occurred and iris undulated, however there was no iris prolapse through the corneal incisions. Intracameral adrenaline was used, however iris hooks had to be resorted to as pupillary size decreased to 3 mm and intracameral adrenaline did not appreciably decrease the IFIS features. The phacoemulsification procedure was completed and intraocular lens was successfully implanted into the capsular bag.

Case 3

A 58-year-old man presented to us for painless progressive decrease in vision in both eyes. Preoperative evaluation showed cataract and poorly dilating iris in both eyes. Systemically, he was on oral amlodipine for hypertension. He also had a history of depression, for which he was on oral imipramine (25 mg once daily) for a year. However, he had discontinued imipramine 2 months prior to presentation. He was scheduled for phacoemulsification in the left eye under local anesthesia. Preoperatively, the pupil dilated to 5.5 mm. During the phacoemulsification procedure, characteristics of IFIS developed and progressive miosis occurred. Intracameral adrenaline and subsequently iris hooks were used because of ineffectiveness of the former. The phacoemulsification procedure was completed and intraocular lens was successfully implanted into the capsular bag.

The cataract surgery could be completed without any intra-operative complication and postoperative vision was 20/20 in all the three patients.

Discussion

It is suggested that tamsulosin and other α-1 AR-blocking agents cause blockage of the α-1 AR in the dilator muscle of the iris.[1] This prevents the iris from dilating and on their long-term use results in disuse atrophy of iris stroma leading to the loss of iris tonicity. This bestows floppy nature to the iris and causes iris billowing and prolapse through the incision.

Intracameral adrenaline has been used successfully to achieve intraoperative dilation of the pupil as well as to increase the tonicity of iris.[5] This consequently reduces the billowing and prolapse of the iris. However, intracameral adrenaline was ineffective in all of our cases. Alternatively, the iris hooks or iris rings can be used successfully to mechanically stretch the pupil and hold the iris.[6] We used iris hooks in two of our patients and found them to be very effective in allowing us to continue with phacoemulsification.

Imipramine continues to be one of the commonly used antidepressant drugs despite its well-documented adverse effects. This is especially seen in developing countries, where the cost of the drugs is important. Imipramine has antagonistic effects on α-1 ARs and agonist at serotonin 5-HT2 receptors, and dopamine D1 and D2 receptors.[7] Its α-1 ARs blocking activity is very prominent, and is responsible for some of the side effects including orthostatic hypotension and high-resting pulse rates.

Imipramine leads to chronic blockage of α-1 ARs of pupillary dilator muscle, which might result in atrophy of the iris stroma and hence can lead to the occurrence of IFIS. Our first patient was on imipramine for a long time over the previous 25 years

but the other two patients were on imipramine for 10 months and 1 year, respectively. Since, this is the first report describing the occurrence of IFIS with imipramine, we cannot be sure of the duration of imipramine therapy required for IFIS. None of our patients had history of taking any of the α1-AR blocking agents. The first patient had diabetes mellitus and was on regular insulin therapy over the previous 15 years while the third patient was hypertensive and was on regular amlodipine therapy for the past 8 years.

The manifestations of IFIS with α1-AR blocking agents can occur within weeks of their first usage and on the other hand, it may occur even years after cessation of adrenergic antagonist therapy.[8,9] This is probably due to the atrophy of the dilator muscle caused due to the chronic usage of the drug, although complex signaling pathways might be involved.[8,9] The latter might be the reason for having occasional occurrence of IFIS after a short course of the incriminated drug. Thus cessation of therapy prior to undergoing cataract surgery is not recommended. In our series of patients, despite discontinuation of imipramine therapy, two of our patients had manifestations of IFIS.

Tamsulosin is highly selective for the α1A adrenoreceptors and hence has very high propensity to cause IFIS. On the other hand, non-selective adrenoreceptor antagonists like terazosin, prazosin doxazosin, alfuzosin are also incriminated in the causation of IFIS, although to a much lesser extent and may exhibit only partly IFIS features.[1,10,11] This was also seen in our second patient, where partial IFIS features were present. Ugarte *et al*.,[2] reported IFIS in a patient on mianserin for 20 years. Mianserin and imipramine are α-1 receptor antagonists and dopamine receptor agonists. Fine *et al*.,[4] reported the occurrence of IFIS in a patient on a dopamine agonist, ropinirole, however the duration of therapy is not mentioned. Ropinirole does not have any antagonist activity on α-1 ARs. Ugarte *et al*.,[2] in their report did not consider the dopamine agonist activity as contributing factor towards IFIS. We speculate that the dopamine agonist activity can also have a contributing role in the occurrence of IFIS, although further research is required to be certain. Diseases like diabetes mellitus and hypertension were thought to have a contributory or causative effect role in IFIS,[6,12] however subsequent studies failed to prove any causative or contributory of either of the diseases in IFIS conclusively.[10,12,13]

Only our first patient was on imipramine at the time of surgery, while other two patients had stopped imipramine 4 months and 2 months prior to cataract surgery, respectively. The second patient had partial features of IFIS unlike the other two patients. Thus, longer the duration of discontinuation of the drug prior to undergoing cataract surgery, milder should be the features of IFIS. Since, this is an anecdotal report, conclusions cannot be drawn based on this report and further research is required to conclusively prove the duration of discontinuation of imipramine required to completely abate the manifestations of IFIS, if at all.

In conclusion, although there is a possible association between IFIS and oral imipramine therapy, it cannot be established based on this case series. This report envisages in making operating surgeons aware of this possible association and thus they can safeguard against IFIS and reduce intra-operative complications due to IFIS.

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