Original Article

A cluster of central retinal artery occlusions following cataract surgery

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Purpose: To report a series of central retinal artery occlusions (CRAO) following cataract surgery complicated by posterior capsular rupture (PCR). **Methods:** Data from 14 patients with acute CRAO following cataract surgery was collected for this study including subject demographics, initial and final best-corrected visual acuity, systemic investigations, optical coherence tomography (OCT) and fundus fluorescein angiography (FFA) findings. **Results:** Mean subject age was 59.9 ± 12.1 years. Male: Female ratio was 1:1. All patients were operated between October and November 2015 and presented with acute vision loss 1 to 4 days after surgery. All the patients underwent cataract surgery under peribulbar anesthesia and had PCR for which anterior vitrectomy (AV) was done. In all the cases Ethylene oxide (ETO) sterilized vitrectomy probe was used for AV. Clinical picture of CRAO was noted in all the cases during the immediate postoperative period. OCT showed inner retinal layer hyperreflectivity while FFA was normal in all the cases. The final visual acuity was poor in all the eyes. This paper discusses the possible mechanisms of CRAO in these cases. **Conclusion:** CRAO is a potential complication of peribulbar anesthesia for intraocular surgery in patients with vascular risk factors and hence any substance that can aggravate the vasospasm in such patients should be used cautiously. Vasospasm could be caused by ETO as residual ETO could be present in the vitrectomy machine tubing causing toxicity. It is recommended to be cautious while using ETO sterilized instruments for cataract surgery.

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1070_18

Quick Response Code:

Key words: Anterior vitrectomy, cataract surgery, central retinal artery occlusion, ethylene oxide sterilization

Central retinal artery occlusion (CRAO) is an acute vascular event that causes painless and sudden visual loss in the affected eye.[1] It is one of the conditions that can lead to permanent vision loss and has been reported after retro bulbar anesthesia in cataract surgery.[2]

The proposed pathophysiology of this complication is direct needle penetration to the optic nerve, drug toxicity, or mechanical compression. To reduce the incidence of such anesthesia-related complications, retro bulbar anesthesia has been largely replaced with other modalities such as topical, intracameral, and peribulbar anesthesia.

Although peribulbar anesthesia avoids direct optic nerve injury, indirect injury presenting as CRAO may occur from vasospasm in response to the injection, a mechanical effect of the volume of anesthetic on the central retinal artery or a vasoconstrictive effect of the anesthetic agent on the central retinal artery.[3,4]

In this observational study, we report a series of 14 patients who developed CRAO after cataract surgery under peribulbar anesthesia within 4 days of surgery. All the patients had posterior capsular rupture (PCR) during surgery for which anterior vitrectomy (AV) was done. Although CRAO after cataract surgery has been reported, it is unusual to get these cases in clusters. On the basis of reported literature and our own experiences with this complication we discuss its possible etiology, including lignocaine-induced vasospasm and spasm due to the use of intracameral adrenaline/adrenaline in the fluid used in the vitrectomy machine or intracameral moxifloxacin or vasospasm caused by residual ETO present in the vitrectomy probe and tubing.

Methods

This study was approved by the Institutional Review Board of our institute. It is a retrospective, observational, single center case series. Medical records of consecutive patients who presented with acute vision loss following cataract surgery performed at the institute between October and November 2015 were reviewed. All the patients presenting with CRAO, which was diagnosed based on typical clinical and OCT features, within few days of cataract surgery were included in the study.

Results

We had performed a total of 22206 cataract surgeries during the 2-month period of which 185 cases had a PCR with vitreous disturbance for which anterior vitrectomy was done.

Out of these, 14 patients presented with acute visual loss 1 to 4 days after cataract surgery.

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Manuscript received: 22.07.18; Revision accepted: 04.01.19

Cite this article as: Sen A, Mitra A, Tripathi S, Sharma M, Shenoy P. A cluster of central retinal artery occlusions following cataract surgery. Indian J Ophthalmol 2019;67:630-3.

All the surgeries were performed under peribulbar anesthesia. Totally, 5 ml of lignocaine without adrenaline was injected with a 26-gauge needle in the inferotemporal quadrant and post injection mechanical pressure was given with a pinky ball for 1 minute in all cases. Three out of 14 patients had undergone phacoemulsification and 11 had undergone manual small incision cataract surgery. All the patients had PCR during surgery for which anterior vitrectomy was done with an ETO sterilized vitrectomy probe. Intracameral adrenaline (0.1 ml of 1:100000 concentration) was used in 6 out of 14 patients due to poor intraoperative dilatation. A rigid Polymethylmethacrylate IntraOcular Lens (IOL) was implanted in the sulcus in 12 out of 14 patients, while in 2 patients IOL could not be implanted due to poor capsular support. The patient characteristics are summarized in Table 1.

The patients presented with loss of vision between 1st and 4th post-operative days and the delay in presentation could be because of difficulty in fundus assessment due to striate keratopathy and corneal edema. Two patients presenting late had moderate to severe striate keratopathy.

All the patients had poor initial visual acuity. Eleven out of 14 patients had a visual acuity of light perception, 2 patients had no light perception and 1 patient had hand movements vision. The visual acuity remained the same till the last follow up. Examination revealed a normal IOP (11-19 mm of Hg) in all instances. All the patients had mild anterior chamber reaction with a quiet vitreous cavity. Fundus examination revealed central retinal whitening akin to CRAO in all the patients except one in which the view was hazy due to corneal edema [Figs. 1a and 2a].

FFA was performed on the first post operative day in 12 out of 14 patients and was essentially normal suggesting re-establishment of retinal blood flow by reperfusion [Figs. 1b and 2b].

OCT was performed in all the patients which revealed hyper-reflectivity of inner retinal layers suggestive of inner retinal ischemia [Figs. 1c and 2c].

Systemic investigations were done for all patients that included blood pressure, random blood sugar, lipid profile, electrocardiogram, and 2D echocardiography to determine any systemic cause for CRAO. Out of the 14 patients, 3 were hypertensive and 2 were diabetics on treatment. All the patients were evaluated thoroughly by the physician for presence of any cardiovascular risk factors.

Discussion

In our case series, OCT revealed hyper-reflectivity of inner retinal layers secondary to ischemic necrosis clinically seen as whitening of the retina suggestive of CRAO. FFA showed a normal arterio venous transit time suggestive of reperfusion, thus concluding that it was a vasospastic rather than a vaso-occlusive event. It showed reperfusion probably because the vascular spasm was transient, but long enough, to cause a CRAO.

Retinal circulation has a marked propensity to reestablish the circulation following an acute retinal artery obstruction and hence visual loss may persist but the fluorescein angiogram can revert to normal at varying times after the insult.

Occlusion of the retinal artery after intraocular surgery with retrobulbar anesthesia has been reported in small cohorts of patients during the past few decades. Although no direct explanation for the vaso-occlusive event was furnished in the pertinent publications, various causative factors were discussed, including iatrogenic injuring of the optic nerve during the injection of the local anesthetic, pharmacological toxicity, or compression of the ocular globe.[2]

Although peribulbar anesthesia avoids direct optic nerve injury, indirect injury presenting as CRAO may occur from vasospasm in response to the injection. It may be a mechanical effect of the volume of anesthetic on the central retinal artery or a vasoconstrictive effect of the anesthetic agent itself on the central retinal artery.[4]

Vinerovsky *et al*. suggested that while the event was likely to be caused by the vasospastic effects of adrenaline, it was also possible to be caused by potential vasospasms in response to the anesthetic injection.[3] Intraoperative ischemia has been reported after retrobulbar blocks.[5] Findl *et al*. reported

Table 1: Baseline patient characteristics, visual acuity, presence of systemic illness and use of intraoperative adrenaline

Patient No.	Age	Sex	Pre-Operative BCVA	Post-Operative BCVA	Systemic illness	Intraoperative adrenaline use
1	60	F	4/60	PL	-	+
2	55	F	1/60	PL	HTN	-
3	76	F	3/60	PL	-	+
4	65	M	5/60	PL	-	+
5	42	F	3/60	PL	DM	+
6	80	F	6/60	PL	-	-
7	40	M	PL PR accurate	PL	-	+
8	58	M	1FFC	No PL	HTN	-
9	73	M	1/60	PL	-	-
10	70	F	6/60	PL	-	+
11	45	M	3/60	PL	DM	-
12	50	F	6/36	HM	-	-
13	65	M	6/36	No PL	HTN	-
14	60	M	3/60	PL	-	-

BCVA: Best corrected visual acuity, DM: Diabetes Mellitus, HTN: Hypertension, HM: Hand movement, FC: Finger Counting, PL: Perception of light, PR: Projection of rays

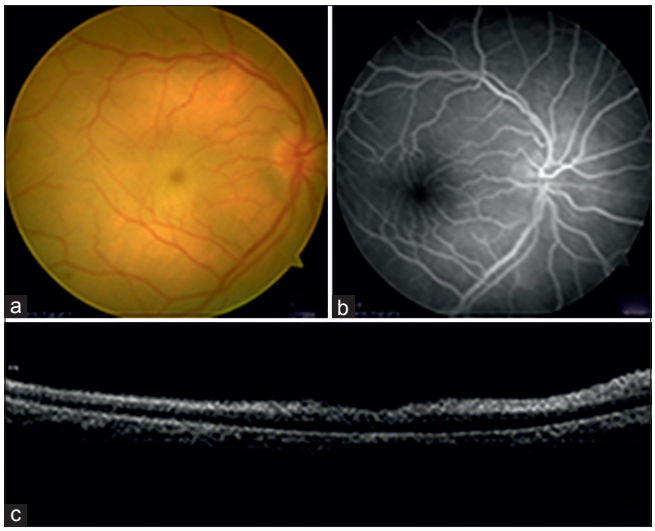

Figure 1: (a) Fundus photograph of patient 1 showing CRAO. (b) FFA of patient 1 demonstrating reperfusion. (c) OCT of patient 1 showing hyperreflectivity of the inner retinal layers

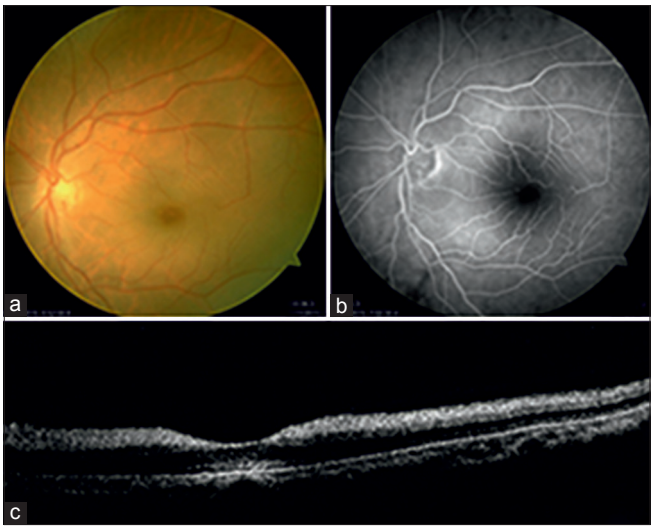

Figure 2: (a) Fundus photograph of patient 2 showing CRAO. (b) FFA of patient 2 demonstrating reperfusion. (c) OCT of patient 2 showing hyperreflectivity of the inner retinal layers

a decrease in retinal blood flow velocity by 15% and 10%, at 1 and 5 minutes, respectively, after peribulbar anesthesia without a vasoconstrictor such as epinephrine.[6]

Occlusion of the central retinal artery may also be caused by increased intraocular pressure (IOP) secondary to globe compression by the anesthetic agent. It is, however, known that extreme and prolonged increase in IOP (over the systolic arteriolar pressure) is needed to produce such retinal artery occlusion. Findl *et al*. found no correlation between the high IOP and a decrease in retinal blood flow following peribulbar injection for cataract surgery.[6] Mechanical effect of bolus anesthetic can lead to elevation of IOP or direct pressure over the vessels. IOP increase may lead to more significant damage in patients with glaucoma as it is associated with deficient blood supply to the optic nerve.[7]

The retinal arterial perfusion depends up on mean arterial pressure and IOP. A fall in mean arterial pressure or rise in IOP may lead to transient cessation of retinal artery perfusion. It is possible that IOP spike intraoperatively or during immediate postoperative period could have led to transient vascular occlusion. Although all the patients had normal IOP at presentation the possibility of transient IOP rise cannot be ruled out.

Pharmacologically mediated changes in the vascular caliber due to the anesthetic agent is another likely mechanism in which retinal artery occlusion can occur. Lidocaine in low concentration causes vasodilation but can cause vasoconstriction in higher doses causing ischemia.[8] Hørven *et al*. demonstrated that the anesthetic solution itself could cause a decrease in blood flow within the ophthalmic artery by exerting a vasoconstrictive effect.[9] Tappenier C *et al*. postulated that the preservatives used in local anesthetics could cause vaso-occlusive events.[10]

In the present case series one possible hypothesis could be transient retinal vascular spasm due to direct seepage of lignocaine from subconjunctival space to the vitreous cavity during vitrectomy. No case in our series had documented subconjunctival ballooning post peribulbar injection that may lead to risk of seepage making that an unlikely cause of the CRAO.

Another possibility is the use of intracameral adrenaline in eyes with posterior capsule rupture could have caused a transient vasospasm. To our knowledge, no previous study reports effect of intracameral adrenaline in increasing the chances of CRAO. Moreover, in our case series only 6 patients had received intracameral Adrenaline, so this could less likely be the cause of CRAO in the present series.

Intracameral moxifloxacin (0.1 ml) was used in all cases. However, this dose has been found to be safe even in cases with PCR with no reports of CRAO post injection. Also the same batch of moxifloxacin was used in many patients on the same day who did not present with these signs making moxifloxacin an unlikely causative factor in this series of CRAO patients.[11]

Hemorrhagic Occlusive Retinal Vasculitis (HORV) has been reported post cataract surgery with vancomycin usage. We performed a dilated fundus and peripheral examination in all patients. None of them showed any evidence of hemorrhages or venular and peripheral involvement, and hence HORV is unlikely in our series.[12]

Could the vasospasm be due to residual ETO on the surface of vitrectomy probe? In the present case series anterior vitrectomy was performed in all the cases. The vitrectomy probes used were all ETO sterilized. It is possible that some chemicals or toxins over the surface of vitrector or within the tubings could have caused the vasospastic event. Unlike a pars plana vitrectomy which utilizes a continuous infusion of the irrigating fluid which would wash out the residual ETO toxins, anterior vitrectomy does not have the benefit of a continuous irrigation which may have caused accumulation of the ETO toxins. Although ETO sterilization has been reported to cause Toxic Anterior Segment Syndrome (TASS), CRAO has not yet been reported to be associated with it.[13]

ETO sterilization has been proven to be safe and free from toxicity if used in correct controlled situations.[14] ETO sterilization uses a toxic gas to alkalinize microorganisms and kill them. ETO gas is preferred for equipment that must be stored sterile and ready for use, although the time necessary

to process through an entire sterilization cycle can be up to 14 hours.[15] ETO sterilized instruments have a lengthy aeration time after each cycle to allow removal of harmful residuals before opening the chamber door. The aeration time varies by manufacturer but can be between 12 and 24 hours. Instruments that must be sterilized using the ETO method can be used only once in a 24-hour period.

As per our sterilization protocol it was routine to use ETO sterilized instruments after an aeration period of 12 hours (in accordance to manufacturer's recommendation). After consultation with experts, we increased the aeration time to 48 hours and rinsed the probes thoroughly with normal saline before use and did not encounter any further CRAO cases post cataract surgery. OCT was done in all cases of PCR occurring during the next 6 months after changing our ETO protocol. However, we did not encounter any similar case after the ETO protocol change. Stoppage of occurrence of CRAO on changing our ETO protocol made us believe that residual ETO on vitrectomy probes could have been responsible for this series of post-operative CRAOs. We noted 185 events of PCR wherein anterior vitrectomy was done, however only 14 out of these had CRAO. This could be explained on the basis that we have used fresh probes in some cases and in others the residual ETO content might not be high enough to cause vascular spasm. Only those cases wherein there was significant residual ETO may have had CRAO. The limitation of this study is that we could not directly prove the causality. Further experimental models can help in conclusively establishing the association.

Conclusion

CRAO is a potential complication post cataract surgery in patients with vascular risk factors. Vasospastic events can cause the CRAO and one potential cause for vasospasm could be residual ETO gas on the instruments and hence caution should be exerted while using ETO sterilized instruments for cataract surgery as residual ETO on vitrectomy probes could be a potential risk factor of CRAO in eyes undergoing anterior vitrectomy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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