Materials in the vitreous during cataract surgery: nature and incidence, with two cases of histological confirmation

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ABSTRACT

Background: To identify and classify materials in the vitreous (MIV) observed during phacoemulsification cataract surgery (phaco).

Design: Prospective, consecutive, observational case series at one ophthalmic day surgery in Sydney, Australia

Participants: 767 consecutive phaco cases. Cases were excluded if there was posterior capsule rupture or vitreous loss intraoperatively.

Methods: For each patient, age, gender, baseline corrected distance visual acuity (CDVA), presence of pseudoexfoliation, nuclear sclerosis grade and phacoemulsification ultrasound time were recorded. The relationship between these variables and MIV was evaluated with regression analysis. Two patients with MIV developed an Acute Intraoperative Rock-hard Eye Syndrome. In these two patients, pars plana needle aspiration of retrolenticular fluid was performed to re-establish normal intraocular pressure. Histology was undertaken to compare this fluid with known lens material retrieved from the Fluid Management System bags in two unrelated cases.

Main outcome measurements: Presence of MIV during phaco.

Results: MIV were observed in either Berger's space or the anterior vitreous (AV) in 386 eyes (50.3% of cases); the majority was putatively lens material (46.5% of all cases). Pigment and OVD were seen in the AV in 9.8% and 1.7% of cases, respectively. Logistic regression analysis demonstrated that higher nuclear sclerosis grade ($p=0.025$), male gender ($p=0.003$), and greater age ($p=0.016$) were predictive of the presence of MIV. Histological assessment with light microscopy and birefringence techniques identified the MIV as lens material.

Conclusion: MIV were seen in 50.3% of phaco cases. It has been histologically demonstrated that lens materials can be introduced into the AV during phaco.

Keywords: Lens, cataract surgery, cataract

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INTRODUCTION

Modern phacoemulsification cataract surgery (phaco) almost always produces excellent surgical and visual outcomes. Despite an intact posterior capsule, materials foreign to the anterior vitreous (AV) are not infrequently visualised in the AV or Berger's space during phaco.¹⁻³

Based on their appearance, previous reports have postulated that these materials are comprised primarily of lens fragments.^{1,3} The only histological investigation of this material in the literature, however, undertaken in 30 patients undergoing combined phaco and vitrectomy surgery, was unable to obtain histological evidence of lens material in the AV.²

The absence of definitive histological evidence has led to ongoing debate regarding the possibility of lenticular fragment access into the vitreous cavity,^{2,4,5} and indeed over whether materials can enter the vitreous at all.² The authors of the previous histological investigation postulated that these commonly observed 'materials' might only be mimickers of lens material, such as titanium fragments shed from the phaco tip due to wear and tear, or AV condensations.²

These materials, termed "Materials In the Vitreous" (MIV) have been commonly observed by our group. In addition to putative lens material, our group has observed putative pigment, ophthalmic viscoelastic device (OVD), and air in the AV. This study was undertaken to determine the incidence, and classify the nature of, MIV observed in the AV during uncomplicated phaco. Further, the study reports two cases of histological examination of MIV and, to our knowledge, the first histological confirmation of lenticular fragments in the AV during uneventful phaco.

METHODS

This study was a prospective, consecutive, single-surgeon cohort study of 767 eyes undergoing phaco at an ophthalmic day surgery centre in Sydney, Australia between January 2010 and December 2012. Cases were excluded if there was a posterior capsule rupture or vitreous loss intraoperatively. Ethics approval was granted by the University of New South Wales, Australia (Approval: HC13220). The procedures and documentation were performed according to the tenets of the Declaration of Helsinki.

Identification and classification of MIV

All patients underwent preoperative assessment according to the operating surgeon's normal protocol, including slit lamp examination and intraocular pressure measurement. Evidence of vitreous condensations, vitreous synergetic cavities, posterior vitreous detachment and pigment in the AV were sought as part of the preoperative workup. If pigment were recognised preoperatively, careful inspection of the fundus and posterior segment for any source of the pigment, such as a retinal tear, evidence of previous trauma, pseudoexfoliation (PXF) and pigment dispersion syndrome was carried out.

The following surgical procedure was employed in all cases: Two clear corneal incisions were made at approximately 80° from each other, aiming to optimise ergonomic comfort for the surgeon. The mainport incision was 2.2-2.4mm, and the sideport 1.5mm. A 5.5mm capsulorrhexis, confirmed by the surgical assistant with calipers, was performed under dispersive OVD. In all procedures, the Infiniti Vision System (Alcon®, Fort Worth, Texas) was utilised. Following nucleus hydrodissection and rotation, the nucleus was removed utilising the phaco stop and chop technique.⁶ During quadrant removal, the aspiration flow rate was fixed at 30 cc/min. Residual cortical fibres were loosened using the "Hydropolish" technique.⁷ Cortical removal

was performed using automated irrigation/aspiration (I/A), followed by manual irrigation of residual cortical fibres on the posterior capsule. Posterior capsular polishing was used when necessary. A hydrophobic, one-piece acrylic intraocular lens (IOL) was implanted using a D-cartridge (Alcon®) by means of a Monarch III IOL Injector (Alcon®).

Once the cortex had been removed to the surgeon's satisfaction, the surgeon and surgical assistant collaboratively evaluated the presence, number and nature of MIV in either Berger's space and/or the AV. This was achieved by direct observation through the cataract surgical operating microscope.

All cases were classified into four putative classes of MIV (lens material, pigment, OVD, and air) based on the appearance of each one (Figure 1). Each had been previously observed by the authors. The presence of each class of MIV, and the phacoemulsification ultrasound time, were recorded. All data were documented immediately by the OR team on a standard proforma in each case.⁸

Further data collected included age, gender, ocular comorbidities, preoperative corrected distance visual acuity (CDVA) and cataract grade as per the Lens Opacities Classification System III (LOCS III).⁹

In the postoperative period, and in the absence of relevant allergies, patients were given ofloxacin, fluorinated steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) topically. The ofloxacin and NSAIDs were ceased at two weeks, and the fluorinated steroids tapered over several weeks.

All patients were evaluated postoperatively for CDVA at one day, one week and one month following phaco. Slit lamp examination and intraocular pressure (IOP)

measurement were carried out at each visit. Postoperative visual acuity assessment was performed with objective laser interferometric refraction. Manual retinoscopy and subjective refraction were performed if necessary. A thorough postoperative ophthalmological examination was repeated in cases where postoperative CDVA did not meet clinical expectations, or if the CDVA deteriorated between the first and subsequent postoperative visits. This examination included detailed inspection of the ocular surface, visual fields to confrontation, pupillary assessment (to exclude a relative afferent pupillary defect), fundus examination and optical coherence tomography (OCT).

Histological investigation of MIV

Two cases of the 767 with MIV experienced Acute Intraoperative Rock-hard Eye Syndrome (AIRES) during phaco.¹⁰ In both cases of AIRES, MIV were visualised. Both cases of AIRES were successfully managed with emergent pars plana needle aspiration of retrolenticular fluid with a 23-gauge needle and a 3 mL syringe.¹⁰ Serendipitously, this facilitated the collection of MIV for histological examination. Samples of the MIV were sent to two independent, consultant histopathologists (CPD and PAM). Both samples underwent haematoxylin and eosin staining, and were assessed using birefringence techniques.

The MIV specimens collected from the AIRES cases were compared with known lens material retrieved from the Fluid Management System (Alcon®) bags from two unrelated cases following phaco.

Statistical analysis

Binary logistic regression analysis was performed to identify any relationship between presence of MIV and age, gender, baseline CDVA, presence of PXF, nuclear

sclerosis grade (LOCS III)⁹ and phaco time. All statistical analyses were performed using SPSS[®] (version 22; SPSS Inc., Chicago, Ill).

RESULTS

The study cohort comprised 767 prospective, consecutive phaco surgeries. All cases were included as posterior capsular rupture or vitreous loss did not occur in any of the cohort. The mean patient age was 70.9 years (SD: 9.1 years) and 61.8% of the cohort was female (474 cases).

Some form of MIV was seen in 386 cases (50.3%). Putative lens material was most commonly observed, being visualised in 357 cases (46.5%) (Figure 1a, b). Pigment MIV was seen in 75 cases (9.8%) (Figure 1c), while OVD MIV was observed in 13 cases (1.7%) (Figure 1d, e). Though the authors have previously seen, and occasionally continue to see, air in the AV, none was seen in the study cohort (Figure 1f). These findings are summarised in Table 1. It should be emphasised that different types of MIV can be observed concurrently (Figure 1 c, d). In our cohort, cortex and pigment MIV were seen concurrently in 60 cases (7.8%); cortex and OVD in 8 cases (1.0%); and cortex, pigment and OVD MIV in 5 cases (0.7%).

Binary logistic regression analysis demonstrated that higher nuclear sclerosis grade ($p=0.025$), male gender ($p=0.003$), and greater age ($p=0.016$) were predictive of the presence of any MIV. Higher nuclear sclerosis grade ($p=0.006$) and male gender ($p=0.010$) predicted the presence of lens material in the AV. Presence of PXF alone predicted pigment in the AV ($p=0.007$). Higher nuclear sclerosis grade alone predicted OVD in the AV ($p=0.019$). Phacoemulsification ultrasound time and baseline CDVA had no significant predictive value for any form of MIV.

Case with cystoid macular oedema

One patient developed clinically significant cystoid macular oedema (CMO). This was diagnosed by a deterioration in CDVA from 6/4 (confirmed at the one day and one week followup) to 6/18 at one month. Fundus examination and OCT confirmed the diagnosis. Treatment led to resolution of this patient's CMO, and CDVA recovered to 6/4 at four months. MIV had not been visualised in this patient.

Histological examination of MIV

Retrolenticular fluid samples containing MIV from each of the two AIRE¹⁰ patients were histologically compared with known lens material derived from the Fluid Management System bags of two unrelated cases. Haematoxylin and eosin staining, and examination under polarized light, demonstrated the MIV to display characteristics identical to the known lens material derived from the bags. It was subsequently concluded that both retrolenticular fluid samples contained lens material (Figures 2a, b, c, d).

DISCUSSION

To our knowledge, this study is the first to provide histological confirmation of the presence of lens material in the AV during routine phaco. Further, this study has identified older age, male gender and more advanced nuclear sclerosis grade as risk factors for MIV. Although MIV has been observed by many cataract surgeons, the high frequency of MIV reported (50.3%) is of a higher rate than the authors believe many surgeons would intuitively estimate.

Phaco of denser nuclei, requiring higher energy output, may contribute to lens fragments moving more vigorously in the anterior chamber. In addition, it is entirely possible that one of the techniques for freeing tenacious cortex, direct irrigation with a straight or a curved cannula of the inferior or superior capsular bag fornix,⁷ may have contributed to this phenomenon. When repeated with a single, potentially powerful jet of balanced salt irrigated through a syringe and a cannula, there may well have been transgression of the zonular apparatus by the balanced salt solution and small pieces of lens material.

As mentioned in the Introduction, it was suggested previously by Liu et al. that materials observed in the vitreous during cataract surgery may be titanium fragments shed from the phaco tip due to wear and tear,² or AV condensations, which, when observed through an operating microscope, may possibly resemble lens material.⁴ The authors can confidently say that at no stage before, during or after this study, have the surgeons in our group seen 'metal' in the AV, nor AV condensations, that could have been confused with the four types of MIV documented by our group.

This study found a high rate of MIV in normal eyes with intact posterior capsules and zonules. It therefore suggests the existence of an anatomical conduit allowing movement of fluid and particulate matter between the anterior chamber and posterior segment in some normal eyes. Indeed, such a conduit has been previously suggested by cases of unexpected staining of the posterior surface of the posterior capsule by trypan blue during phaco in normal eyes.¹¹ However, to our knowledge, this has yet to be formally identified anatomically.

It is postulated that the conduit by which MIV enter the vitreous cavity is through the interstices between the intact zonular fibres during nuclear phacoemulsification and cortical I/A. Such a conduit would also account for the retrolenticular misdirection of fluid associated with the phenomenon of AIRES.¹⁰ The authors emphasise that such a conduit exists in the absence of zonular deficiencies, as no cases in our cohort were noted to have intraoperative zonular instability.

The risk factors for MIV identified in this study were higher nuclear sclerosis grade, male gender, age, and in the case of pigment MIV, the presence of PXF. These risk factors are also associated with zonular dehiscence and weakness.^{12,13} This suggests that in patients with these risk factors, the zonular fibres may be physically or biochemically altered. This occurs despite them appearing normal under the operating microscope, and demonstrating no axial shift of the capsulorrhexis margin. This zonular fibre alteration may allow anterior segment materials to bypass the zonular fibres more readily, and enter the posterior segment, resulting in MIV. Supporting this notion are previous case reports of inadvertent staining of the vitreous with trypan blue during phaco. This has been observed in eyes where previous ocular trauma or pre-existing PXF have caused zonular apparatus weakness.¹⁴⁻¹⁷

Further, a report out of Manchester, England, documented a case in which anterior capsular irrigation with trypan blue led to blue discolouration of the posterior surface of the posterior capsule in a previously vitrectomised patient.¹⁸ Indeed, the authors' vitreoretinal colleagues report this as a not infrequent occurrence. In the current study cohort, one patient who had previously undergone vitrectomy likewise developed blue discolouration of the posterior surface of the posterior capsule following anterior capsular irrigation with trypan blue. Interestingly, in this case, following gentle balanced salt irrigation continued over three more minutes, there was near complete resolution of the blue posterior capsule discolouration. The surgery was then completed uneventfully. This represents further indirect evidence of the anatomic conduit between the anterior chamber and the vitreous cavity.

CMO is recognised as one of the leading causes of poor visual outcomes after uncomplicated phaco, and may result in permanent visual loss.¹⁹ The pathogenesis of CMO is considered most likely to be inflammatory.²⁰⁻²³ Inflammation may result in disruption of the blood-aqueous barrier with a subsequent increase in iris vascular leakage and disruption of the blood-retinal barrier.²⁰⁻²³ The posterior segment of the eye is normally not exposed to lens antigens, as is the case with the other intraocular structures. As MIV are foreign to the posterior segment, they therefore represent a potential new immunological stimulus, to which the posterior segment is naive. They may therefore contribute to intraocular inflammation following cataract surgery. Moreover, the ingress of macroscopic MIV suggests that other, microscopic materials released during phacoemulsification, such as free radicals or lens epithelial cells, may also be introduced into the vitreous.²⁴⁻²⁷ These materials may possibly play a role in postoperative complications.

The one case of CMO encountered in our study was not associated with MIV. Due to the small size and low rate of clinically significant CMO (1 of 767, 0.13%) in the

study cohort, however, our study was not adequately powered to examine the relationship between MIV and CMO. As such, the authors are unable to draw conclusions as to the significance of MIV in relation to postoperative complications.

Thus, the presence of MIV demonstrates the existence of a conduit between the anterior and posterior segments of the eye, and may be associated with physically altered or biochemically altered zonular fibres. Therefore, in cases where MIV are observed, it may be helpful for surgeons to exercise increased care when completing the phaco, especially when irrigating with balanced salt solution. MIV may also suggest the need for increased vigilance in postoperative management, and particularly for surgery on the second eye.

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In conclusion, this study has demonstrated that MIV may be observed in as many as 50.3% of uncomplicated phaco cases. MIV consists mainly of lens material, but pigment and OVD were also recognised. Although the authors have previously and subsequently observed air in the AV, no air was visualised in this study cohort. Age, male gender and higher nuclear sclerosis grade were predictive of MIV. The finding of PXP was predictive of pigment MIV. Confirmation that the histological nature of MIV was lens material was obtained in two cases. Further studies may elucidate of the significance of MIV in operative and postoperative phaco complications.

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FIGURE LEGENDS

Figure 1:

- a. Single piece of lens material (arrow) in the anterior vitreous during phacoemulsification cataract surgery.
- b. Multiple pieces of lens material noted in the anterior vitreous towards completion of irrigation/aspiration in a grade 4 nuclear sclerotic cataract. Note residual subincisional cortex is still to be removed.
- c. Pigment (thick arrows) along with lens material (thin arrow) in the anterior vitreous.
- d. Lens material (thick arrow) and OVD (thin arrow) in the anterior vitreous.
- e. Lens material (thick arrow) and OVD (thin arrow) in the anterior vitreous. Note that in panel e, the lens material and the OVD have moved relative to each other within the anterior vitreous (compared with d).
- f. Six discrete air bubbles seen in the anterior vitreous during uneventful phacoemulsification cataract surgery. Their location is confirmed as this image was taken immediately prior to inflation of the anterior chamber with balanced salt solution at the completion of surgery. Posterior capsular folds are seen anterior to the air bubbles in the anterior vitreous. Air was not observed in the study cohort. This photograph was taken during surgery on a patient with a LOCS III grade 2+ cataract in September 2015. This patient's corrected distance visual acuity was 6/4 at one day, one week and one month postoperatively.

Figure 2:

a, b. Light microscopy (haematoxylin and eosin [x100]) showing the histology of the material in the vitreous obtained from retrolenticular fluid, consistent with known lens material.

c, d. Haematoxylin and eosin (x100) with polarised light showing the material in the vitreous. Both of these specimens demonstrated the same haematoxylin and eosin staining and birefringence as lens material obtained from the Fluid Management System bags.

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TABLE

Table 1: Classification and incidence of materials in the vitreous (MIV).

Type of MIV	Frequency (n)	Incidence (%)
Lens material	357	46.5%
Pigment	75	9.8%
OVD	13	1.7%
Air	0	0.0%

OVD = Ophthalmic Viscoelastic Device.

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