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ORIGINAL PAPER

Phacoemulsification cataract surgery in patients receiving novel oral anticoagulant medications

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Abstract

Introduction An increasing number of patients are taking novel oral anticoagulant (NOAC) medication, making perioperative management in phacoemulsification surgery an important issue. This study reports the haemorrhagic complications of NOAC in phacoemulsification surgery.

Design Retrospective case study over a 4-year period.

Methods Consecutive cases receiving NOAC during the time of phacoemulsification were reviewed. Patients were either advised to continue medications (continued group) or withhold medications before surgery (withheld group).

Main outcome measures Details including patient demographics, preoperative assessment, postoperative outcome and intraoperative, postoperative and systemic complications were recorded.

Results A total of 20,100 cases of phacoemulsification were performed. Of which, 66 cases were found to be on NOAC (0.33%). This included 66 eyes of 53 patients, with 42 continued and 24 withheld medications before surgery. There was no statistically significant difference between the two groups in demographics, cataract risk factors, baseline renal function, clotting profile, type of NOAC, incision size, phacoemulsification energy, preoperative and postoperative visual acuity. There was also no significant difference in intraoperative, postoperative and systemic complications ($p = 1.00$ and 0.53, Fischer's exact test). None of the patients in the continued group had postoperative complications; two cases in the withheld group receiving retrobulbar anaesthesia had bruising and subconjunctival haemorrhage after resumption of NOAC ($p = 0.13$, Fischer's exact test).

Conclusion The present study found no difference in haemorrhagic complications between cases continuing and withholding NOAC during phacoemulsification. Nevertheless, the potential risks and benefits to continue or withhold NOAC perioperatively should be carefully considered via a multidisciplinary approach.

Keywords NOAC · Novel oral anticoagulant · Phacoemulsification · Cataract · Haemorrhagic complication · Perioperative · Non-vitamin K antagonist oral anticoagulants

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Introduction

In order to lower thromboembolic risks, increasing number of patients with cardiovascular, cerebrovascular or cardiac arrhythmic diseases are being prescribed antiplatelet or anticoagulant medications. More recently, a new class of novel oral anticoagulant (NOAC) medications, also known as non-vitamin K antagonist oral anticoagulants [1], has been introduced to clinical practice and has been gaining popularity. Although VKA has a long history of clinical use and is proven to be effective and safe within therapeutic range [2, 3], its use is limited by the need for frequent blood taking for monitoring, interference from diet [4] and underutilization [5]. In contrast, the NOAC group of medications directly yet reversibly targets the clotting cascade, inhibiting thrombin (dabigatran) or factor Xa (apixaban and rivaroxaban) which means less interaction with diet and other medications, more rapid onset, faster reversibility and avoids the need for frequent monitoring. Despite the many advantages NOAC has over VKA, limitations still exist, for example, the lack of an effective antidote for immediate drug reversal [6] and readily available sensitive laboratory tests for measuring its therapeutic effect.

Phacoemulsification is a commonly performed ophthalmic surgery among the elderly patient population, among which are also the most prone to thromboembolic risks and most likely to require risk reduction medications. Suprachoroidal haemorrhage is a rare, but potentially visually devastating complication of cataract surgery. The incidence was found to be 0.03% in phacoemulsification surgery [7], and use of cardiac medications is a significant independent risk factor[8]. Although both intraoperative and postoperative haemorrhagic complications are rare, patients on antiplatelet and warfarin medications undergoing cataract surgery by phacoemulsification do carry a low risk of intraocular bleeding [9–11]. Although the continuous use of antiplatelet and anticoagulants in cataract surgery appears safe, the final decision whether to stop medication depends on the risk benefit ratio [12]. Furthermore, little evidence is available in the current literature on the risks and complications of continuing the new class of NOAC medication in patients undergoing phacoemulsification surgery. A recent online survey among vitreoretinal surgeons in the UK showed that 83% of surgeons were unsure of the preoperative management of patients on NOAC [13]. This study aims to investigate the safety and risks of NOAC in phacoemulsification surgery.

Materials and methods

A retrospective review of electronic patient records of consecutive patients on three types of NOAC medications (dabigatran, rivaroxaban and apixaban) undergoing phacoemulsification and intraocular lens implantation during the study period of January 2012 to September 2016 at the Kowloon East Ophthalmic Service, Hospital Authority, Hong Kong was conducted. The Kowloon East Ophthalmic Service serves the eastern peninsula of Kowloon with a population of around 1 million. At the preoperative assessment clinic, patients were advised to either continue their NOAC medications or withhold the medications during the time of surgery, based on the ophthalmologists' discretion. Patients were divided into the continued group or withheld group depending if NOAC was continued or withheld during the time of phacoemulsification surgery. In patients who withheld NOAC, this was liaised with the patient's medical physician.

Patient demographics, type of NOAC, renal function, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), type of cataract, operative risk factors, mode of anaesthesia, phacoemulsification ultrasound energy utilized, preoperative, postoperative visual acuities, intraoperative and postoperative complications and systemic complications within 1 month were all recorded.

Only cataract surgeries performed using phacoemulsification were included. The surgery was done either under topical anaesthesia with 2% lidocaine gel and provaine eye drops, retrobulbar, peribulbar or subtenon anaesthesia with 2% lignocaine. Phacoemulsification was performed using the Infiniti Vision System (Alcon Laboratories, Forth Worth, TX, USA). Intracameral cefuroxime (1 mg in 0.1 ml) was injected at closing of surgery in all cases without any contraindications, as previously described [14]. A combination ointment of antibiotics and steroids was applied in addition to eye pad and eye shield postoperatively. Patients were seen at 1 day, 1 week and 1 month postoperatively, unless more frequent follow-up was required.

Statistical analysis was performed with SPSS software version 22 (SPSS, Inc., Chicago, IL, USA). The level of significance was set at $p < 0.05$. For continuous variables such as age, the mean was calculated and the two-tailed student *t* test under equal variance was used to test for statistical significance. However, normality assumptions were not satisfied for mean logMAR visual acuity, baseline renal function and clotting profile, and the Mann–Whitney test had to be used instead. For the categorical variables of laterality, gender and age, proportions were calculated and Pearson Chi-square was used to test for statistical significance. Due to low expected cell counts in the 2×2 tables for baseline ocular risk factors, mode of anaesthesia, NOAC medications and postoperative complications, Fisher's exact test had to be used instead.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the local Institutional Review Board (IRB) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Results

During the study period, a total of 20,100 cases of phacoemulsification were performed at the Kowloon East Ophthalmic Service. The number of cases on NOAC accounted for 0.33% of cases (66/20,100). A total of 66 eyes (29 male, 37 female) taking NOAC received phacoemulsification surgery. Forty-two cases were continued on NOAC throughout surgery (continued group), and 24 cases withheld NOAC before surgery and resumed the medication postoperatively (withheld group). The mean duration of withholding NOAC was 2.67 ± 1.52 days. When comparing the continued and withheld group, there was no statistically significant difference in demographics including laterality, gender and mean age (Table 1).

During the preoperative assessment, there was no statistically significant difference in surgical risk factors, including cataract density, pupil size and anterior chamber depth between the two groups (Table 2). For the mode of anaesthesia, the majority was performed under topical anaesthesia (77.3%), followed by retrobulbar anaesthesia (16.7%), peribulbar anaesthesia (1.5%) and posterior subtenon anaesthesia (1.5%). There was statistically significant difference in the use of topical anaesthesia between the continued group and withheld group (90% versus 15%, $p = 0.01$, Fischer's exact test) (Table 3).

Table 1 Patient demographics

	Continued (SD)	Withheld (SD)	*p* value
Age (years)[a]	79.5 (4.25)	78 (9.5)	0.39[c]
Laterality[b]			1[d]
Right eye	21 (50)	12 (50)	
Left eye	21 (50)	12 (50)	
Gender[b]			0.43[d]
Male	20 (47.6)	9 (37.5)	
Female	22 (52.4)	15 (62.5)	

[a]Data are presented as median (interquartile range): age

[b]Data are presented as *n* (%): laterality, gender

[c]Assessing by Mann–Whitney *U* test

[d]Assessing by Chi-square test

Among the 66 cases, 48.5% were taking dabigatran, 47% were taking rivaroxaban and only 4.5% were prescribed with apixaban. Aspirin was concurrently prescribed in two cases in the continued group and in three cases in the withheld group ($p = 0.35$, Fischer's exact test). There was no statistically significant difference in the type of NOAC medications prescribed between the continued and withheld group (Table 4).

There was significant difference in baseline creatinine ($p = 0.04$, Mann–Whitney *U* test) but not urea between the two groups (Table 5). Baseline prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ration (INR) were not statistically significantly different between the two groups ($p = 0.91/0.10/0.43$, Man Whitney *U* test).

Regarding the phacoemulsification surgery itself, the mean wound size was 2.50 in the continued group and 2.56 in the withheld group ($p = 0.37$, Mann–Whitney *U* test). The mean ultrasound energy used during phacoemulsification surgery was comparable between the two groups, 16.27 s in the continued group and 22.39 s in the withheld group ($p = 0.26$, Mann–Whitney *U* test). The postoperative logMAR visual acuity at 3 months was not significantly different ($p = 0.13$, Fisher's exact test). The haemorrhagic

Table 2 Baseline ocular risk factors and visual acuity

	Continued (SD)	Withheld (SD)	*p* value
Preoperative logMAR visual acuity[a]	0.52 (0.21)	0.61 (1.29)	0.20[c]
Cataract density[b]			0.16[d]
Soft	4 (9.8)	5 (25)	
Moderate	27 (65.9)	9 (45)	
Hard	10 (24.4)	5 (25)	
Very hard	0 (0)	1 (5)	
Pupil size[b]			0.07[d]
Well dilated	38 (92.7)	18 (75)	
Poorly dilated	3 (7.3)	5 (20.8)	
Small pupil	0 (0)	1 (4.2)	
Anterior chamber depth[b]			0.30[d]
Normal	31 (77.5)	21 (91.3)	
Shallow	9 (22.5)	2 (8.7)	

[a]Data are presented as median (interquartile range): preoperative logMAR visual acuity

[b]Data are presented as *n* (%): cataract density, pupil size and anterior chamber depth

[c]Mann–Whitney *U* test

[d]Fisher's exact test

Table 3 Mode of anaesthesia

	Continued	Withheld	*p* value[b]
Anaesthesia[a]			0.01*
Topical	33 (82.5)	15 (62.5)	
Retrobulbar	3 (7.5)	8 (33.3)	
Peribulbar	0 (0)	1 (4.2)	
Posterior subtenon	1 (2.5)	0 (0)	
Monitored	3 (7.5)	0 (0)	

[a]Data are presented as n (%): mode of anaesthesia

[b]Fisher's exact test

*Significance at 0.05

complication rate in the continued group was 0%, while it was 8.3% in the withheld group (Table 6).

The two cases with haemorrhagic-related complications included one case with right forehead bruising and another case with left eye periorbital bruising and subconjunctival haemorrhage. Both cases were done under retrobulbar anaesthesia and the haemorrhagic events occurred after resumption of NOAC. One case in the continued group had acute exacerbation of chronic obstructive pulmonary disease (COPD) and developed fast atrial fibrillation (AF) 4 days after phacoemulsification surgery. No patients had any thromboembolic events. None of the patients had intraoperative complications.

Discussion

Previous studies investigating the safety of antiplatelet and anticoagulant medications during phacoemulsification surgery found it safe in uncomplicated cataract surgeries, especially when performed under topical anaesthesia [10, 11, 15]. The American College of Chest Physicians suggests continuation of aspirin and warfarin during cataract surgery in view of the avascular nature of the procedure [16].

The NOAC class of medications has the advantage of shorter half-life when compared with warfarin and can be stopped 48 h before procedure. Although each NOAC medication has different effects on PT, INR and aPTT, unlike warfarin and heparin, these tests cannot be used to monitor their actual anti-coagulating effects. The results of the present study also confirmed

Table 4 NOCA medication

	Continued (SD)	Withheld (SD)	*p* value[b]
NOCA medication[a]			0.25
Dabigatran	23 (54.8)	9 (37.5)	
Rivaroxaban	18 (42.9)	13 (54.2)	
Apixaban	1 (2.4)	2 (8.3)	

[a]Data are presented as *n* (%): NOAC medication

[b]Fisher's exact test

Table 5 Baseline renal function and clotting profile

	Continued (SD)	Withheld (SD)	*p* value[b]
Creatinine (umol/l)[a]	93 (34.00)	83 (32.75)	0.04*
Urea (umol/l)[a]	5.8 (3.48)	6 (2.95)	0.28
Prothrombin time (PT) (s)[a]	13.2 (2.50)	13 (3.48)	0.91
Activated partial thromboplastin time (aPTT) (s)[a]	34.5 (12.15)	30.7 (7.70)	0.10
International normalized ratio (INR) (s)[a]	1.2 (0.20)	1.1 (0.28)	0.43

[a]Date are presented as median (interquartile range): creatinine, urea, prothrombin time, aPTT and INR

[b]Mann–Whitney *U* test

*Significance at 0.05

Table 6 Postoperative complications and visual acuity

	Continued	Withheld	*p* value
Complications[a]			
Intraoperative	0 (0)	0 (0)	1[c]
Postoperative haemorrhagic	0 (0)	2 (8.3)	0.13[c]
Postoperative non-haemorrhagic	0 (0)	0 (0)	1[c]
Systemic	2 (4.8)	0 (0)	0.53[c]
Postoperative logMAR visual acuity (3 months)[b]	0.22 (0.24)	0.30 (0.18)	0.15[d]

[a]Date are presented as *n* (%): complications

[b]Date are presented as median (interquartile range): postoperative logMAR visual acuity (3 months)

[c]Fisher's exact test

[d]Mann–Whitney *U* test

there was no difference in the PT, INR and aPTT levels between the continued and withheld groups. As no effective antidote is available and its clearance can be affected by renal function, the decision on the duration of discontinuation should be made after checking for serum creatinine levels. The randomized evaluation of long-term anticoagulation therapy (RE-LY)-randomized trial studied the periprocedural bleeding rates in a number of surgical procedures, including cataract surgery, but did not find any significant difference between dabigatran and warfarin, while dabigatran allowed a shorter duration of interruption [17]. The European Heart Rhythm Association published a practical guide for non-valvular atrial fibrillation and suggested that in procedures that carry 'no clinically important bleeding risks' such as cataract and glaucoma surgery, NOAC can be taken at its trough level (i.e. 12 or 24 h after last intake), or skip one dose (i.e. 18–24 h after last intake) and restart 6 h later [18]. The mean duration of stopping NOAC was 2.67 days in the present study. The short interval of drug interruption may explain the low rate of systemic complications. None of the patients had systemic complications in the withheld group. The patient who developed fast AF was in the continued group, likely due to acute exacerbation of COPD itself.

In the present study, there were no intraoperative or postoperative haemorrhagic complications in the continued group, whereas two patients in the withheld group had haemorrhagic-related complications. However, both were minor and self-limiting including subcutaneous bruising and subconjunctival haemorrhage, which occurred after resuming NOAC postoperatively. Both cases were done under retrobulbar anaesthesia. There were no haemorrhagic complications among cases done under topical anaesthesia alone. The haemorrhagic risk of retrobulbar anaesthesia was shown to be less than one per 100 procedures

and suggested to be low even in patients on anticoagulation [19]. Although the Royal College of Ophthalmologists in the UK is against the withdrawal of antiplatelet and anticoagulants prior to cataract surgery, they concluded that firm conclusions cannot be drawn on sight-threatening haemorrhagic complications of regional anaesthesia, based on currently available evidence. Although the present study showed continued use of NOAC in retrobulbar anaesthesia (4.7%) and posterior subtenon anaesthesia (1.6%) did not have any bleeding episodes, the numbers are too small to draw any conclusion and the use of NOAC in regional anaesthesia will require further investigation.

The present study provided some evidence suggesting the continued use of NOAC in phacoemulsification is safe. If one has to contemplate suspending NOAC, it is important to consider other factors. Firstly, there is the risk of thromboembolic events after suspending NOAC. The ROCKET AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibitor Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) [20, 21] trial showed that both patients on rivaroxaban and warfarin had increased risk of stroke and systemic embolism after temporary or permanently stopping their medication. The risk of a major cardiovascular event, including death, after temporarily stopping NOAC was 0.66–1%. The use of bridging therapy with low molecular weight heparin has been suggested for patients with high thrombotic risk [22]. In the present study, all cases in the withheld group were assessed for suitability for suspension of NOAC. The NOAC suspension period and, if required, bridging regimen was prescribed and monitored by internal physicians. Therefore, close communication and collaboration with internal physicians in the perioperative management of NOAC patients undergoing cataract surgery is imperative.

Secondly, we need to assess the risk of bleeding during the surgical procedure. Modern cataract surgery via clear corneal incision is virtually bloodless, but bleeding is sometimes encountered when surgical manipulation of the iris is required, especially in small pupil cases. The present study included small pupil cases, accounting for 13.6% (Table 2). However, none of the poorly dilated pupil cases in the continued group required surgical enlargement of their pupils. Thus, we cannot draw any conclusion on the continuous use of NOAC in cases requiring surgical manipulation of the iris. Although there are many non-surgical ways to increase pupil size both preoperatively and intraoperatively, a short period of suspension of NOAC may be required in complex cases where significant surgical manipulation of the iris is anticipated.

Lastly, our study suffers all the limitations of retrospective study, with its relatively small sample size and non-randomized nature. Prospective study with large sample size is warranted to study the risk of bleeding in patients taking NOAC and undergoing cataract surgery, especially under regional anaesthesia.

Conclusion

The present study demonstrates there is no significant difference in haemorrhagic complications between continuing and withholding NOAC perioperatively in phacoemulsification surgery. The continued use of NOAC appears safe in phacoemulsification surgery. A short interval of interruption when deemed necessary also appears to be safe. Nevertheless, the choice to continue or withhold NOAC perioperatively should be balanced with the benefits and potential risks of thromboembolism and surgical bleeding via a multidisciplinary approach.

What was known

- Current evidence and guidelines suggest the continuous use of antiplatelet and traditional vitamin K anti-coagulants, such as warfarin, in routine phacoemulsification surgery is safe.
- There is little evidence reporting on the risks of intraoperative and postoperative bleeding of a new class of anticoagulants, known as novel oral anticoagulants (NOAC), in cataract surgery. Many ophthalmologists are not familiar with this new class of anticoagulant.

What this paper adds

- We found no statistically significant difference in the haemorrhagic complications, by comparing

consecutive cases continuing and withholding NOAC before phacoemulsification.
- The continued use of NOAC appeared safe in phacoemulsification surgery. A short interval of interruption when deemed necessary also appears to be safe.
- This paper also illustrates the importance of multidisciplinary approach of the management of patients on NOAC undergoing cataract surgery.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study protocol was approved by the local institutional research ethics committee, Institutional Review Board of the Hospital Authority Kowloon East Cluster (reference number KC/KE-17-0117/ER-4). The study firmly adhered to the tenets of the 1964 Helsinki Declaration and its later amendments. For this type of study, formal consent is not required.

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