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TITLE: Warfarin in Vitreoretinal surgery – a case controlled series

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KEYWORDS

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Abstract

Introduction

Warfarin is a commonly used anticoagulant whose effect in Vitreoretinal surgery has not been well studied.

Methods

A series of 60 patients on warfarin therapy undergoing pars plana vitrectomy were retrospectively case controlled to 60 patients with similar presenting complaints. In addition an online survey was performed of current practice in the UK.

Results

2% of the patients receiving vitrectomy were on warfarin. There were 33 males and 27 females with a median age of 72.5 years, follow up was for a mean of 0.88 years. INR ranged between 0.94 to 4.6 (median 2.3). Two cases of suprachoroidal haemorrhages occurred in the control group (one with preoperative choroidal haemorrhage from dislocated lens nucleus), whilst none occurred in the warfarin group. 12 patients with rhegmatogenous retinal detachment in the warfarin group presented with vitreous haemorrhage compared to only four in the control group ($P=0.04$). From the online survey, 48 respondents (81%) would ask patients to withhold warfarin prior to vitreoretinal surgery based on the INR.

Conclusions

There was no increase in complications in patients continuing to take warfarin compared with controls. Patients with RRD are more likely to have vitreous haemorrhage at presentation if they are on warfarin.

INTRODUCTION

Warfarin is an anticoagulant commonly used in patients with mechanical prosthetic heart valves, chronic atrial fibrillation and venous thrombo-embolism. The vitreoretinal surgeon is likely to encounter more patients on this drug because an aging population is associated with an increased number of patients taking warfarin. In general, older patients (over 65 years old) are more than twice as likely to have any surgical operation therefore the effects of warfarin on increased complications during surgery is a risk¹. With ophthalmic surgery, there is a perceived risk of ocular haemorrhage², and some authorities advocate modifying warfarin therapy in certain cases of ophthalmic surgery³. The absolute risk of a thrombo-embolic event in patients undergoing any surgical procedure who interrupt warfarin for between 6-8 days preoperatively ranges from 0.02% in low risk patients with atrial fibrillation to 0.42% in patients with prosthetic heart valves⁴. For ophthalmic surgery, in particular vitreoretinal surgery, there is no consensus with regard to the risks or benefits of discontinuation of warfarin in the perioperative period. This study was therefore designed to compare presenting features and outcomes of pars plana vitrectomy surgery in patients anticoagulated with warfarin compared to case controls. Additionally, we surveyed members of the British & Eire Association of Vitreoretinal Surgeons (BEAVRS) to gather a consensus of current trends amongst its members.

METHODS

All vitreoretinal procedures performed or supervised by one author (THW) are entered onto an electronic patient record database (available with Vitreoretinal Surgery published by Springer)⁵. In this database all peri-operative complications are prospectively recorded. Patients who were taking warfarin were asked to continue their anticoagulation during the surgical period. Patients receiving pars plana vitrectomy (PPV) between January 2001 and December 2008 were examined with only the first operation for each patient included for analysis. These patients were case controlled to patients on the database for age, sex and presenting complaint. Patients taking aspirin or other antiplatelet agents were excluded from this study. Their demographics, ocular history and examination,

presentation, severity of vitreous haemorrhage at presentation, number of vitreoretinal procedures, visual outcome and complication rates were collected. Approval was obtained from the institutional research ethics committee of Guy's & St. Thomas' Hospitals NHS Foundation Trust and the study conformed to the declaration of Helsinki. Informed consent was obtained from all patients. Direct comparative analyses were performed using paired T test, MacNemar test and Mann Whitney matched pair test as required using Analyse It software.

An online survey (www.freeonlinesurvey.com) was sent to all registered members of BEAVRS (see appendix). Reminder emails were sent two weeks after the initial requests were sent. The online survey was open for 10 weeks over September till December 2009.

RESULTS

The study period was 2001 to 2008 60 consecutive patients were taking warfarin on the day of pars plana vitrectomy (2% of the patients receiving vitrectomy in this period). There were 33 males and 27 females with a median age of 72.5 years (37.7 years – 89.5 years). Follow up was for a mean of 0.88 years. INR ranged between 0.94 to 4.6 (median 2.3). 6.5% were subtherapeutic (INR <1.49), 19.6% were borderline therapeutic (INR 1.5 – 1.99), 32.6% were therapeutic (INR 2 – 2.49) and 41.3% were high therapeutic (INR > 2.5). Case matched controls, not taking warfarin, had a median age of 71.9 years (13.04-88.3 years), not significantly different from the case group (P=0.277) and were followed up for a mean of 1.06 years. 46 (76.7%) of the patients in the warfarin arm were operated under a general anaesthetic, compared to 34 (56.7%) in the control arm. All local anaesthetics were administered via subtenons. As cases and controls were collected over the same period, surgical techniques were similar between both groups. Indications for vitrectomy included retinal detachment (n=30), vitreous haemorrhage (n=15), macula pucker (n=6), macula hole (n=5), dropped nucleus (n=3) and “other” (n=1) in both groups.

Mean visual acuity improved from logMar 1.3 to logMar 0.69 at final follow up in the control group. Mean visual acuity improved from 1.1 to 0.8 in the warfarin group. There was no significant difference between either initial visual acuity (P=0.172) and final visual acuity (P=0.568). Mean

difference in visual acuity, pre and post operation, was 0.469 (warfarin group) and 0.605 (control group), which was not significantly different ($P=0.282$).

Two cases of suprachoroidal haemorrhages occurred in the control group, whilst none occurred in the warfarin group ($p=0.479$). The first case of suprachoroidal haemorrhage occurred in an 87 year old arteriopathic male who had had a vitreous haemorrhage secondary to neovascularisation in response to an ischaemic hemiretinal vein occlusion. He developed a suprachoroidal haemorrhage during vitrectomy for the vitreous haemorrhage. This gentleman subsequently underwent cataract surgery and developed the same complication during this operation. The second case occurred in an 83 year old patient who had had a dropped nucleus during cataract surgery. A previtrectomy ultrasound examination showed evidence of suprachoroidal haemorrhage, suggesting that this was therefore not necessarily a complication of the vitrectomy.

Five patients in the warfarin group required further PPVs in comparison to 11 in the control group which was not significantly different.

There were 30 cases of retinal detachments in either group: 28 Rhegmatogenous (RRD) and 2 tractional. All of the patients with tractional detachment presented with vitreous haemorrhage in addition. Twelve cases out of the 28 RRD in the warfarin group presented with vitreous haemorrhage compared to only four in the control group. Vitreous haemorrhage as a presenting feature of RRD was therefore significantly higher in the warfarin group ($P=0.04$). Four of the patients in the warfarin group with RRD ultimately had persistent retinal detachments, compared to one in the control group at the last follow up (not statistically significant).

The online survey yielded responses from 59 out of 149 members contacted. 51 of these (86.4%) were at consultant level. With regard to warfarin use, 48 respondents (81%) would ask patients to withhold warfarin prior to vitreoretinal surgery based on the INR. 12 (25%) of these 48 would do so for patients with $\text{INR} > 3.5$ with the rest stopping for lower INR values. 71% of respondents who withheld warfarin stratified the thrombotic risk of the patient by assessing risk factors such as a Cerebrovascular event within the last month, left ventricular dysfunction, age > 75 years,

hypertension, diabetes mellitus, history of venous thromboembolism, active cancer, antiphospholipid syndrome or any mitral valve caged ball⁴.

DISCUSSION

Warfarin therapy is commonly used in patients at risk of thrombo-embolism. Surgeons considering modifying warfarin treatment need to risk stratify their patients based on the indications for anticoagulation⁴. Stopping anticoagulation should be undertaken with care and due consideration must be given to the benefits of such a course of action. It has been suggested that the effects of platelets, drugs affecting platelet function and other factors influencing primary haemostasis have a greater impact on minute surgical trauma, as in ophthalmic surgery, than indirect anticoagulants which influence clotting factors, such as warfarin⁶. Our previous experience has indeed suggested that antiplatelet medication clopidogrel, can be associated with to ophthalmic haemorrhagic complications⁷. Flaxel⁸ reported 3 cases with haemorrhagic complications during vitrectomy which they attributed to aspirin but we have previously found no association of aspirin with increased complications in a cohort study⁹.

Tabendeh *et al*¹⁰ reviewed 32 patients who suffered suprachoroidal haemorrhage during pars plana vitrectomy (PPV). None of these patients were taking warfarin, and only one patient was taking aspirin. Other reviews of 13 cases¹¹ and 12 cases¹² of suprachoroidal haemorrhage during PPV similarly did not show warfarin to being a significant risk factor in the aetiology. We had no difference in intraoperative suprachoroidal haemorrhage rates between patients taking warfarin and controls.

The rate of suprachoroidal haemorrhage in pars plana vitrectomy has not been clarified. Ghoraba¹³ reviewed 3342 pars plana vitrectomies revealing 2 intraoperative suprachoroidal haemorrhages – a rate of 0.06%. Such a retrospective analysis is however very likely to under estimate the complication rate as small bleeds may not be recorded and it is likely that a prospective recording of the complication will uncover a higher rate. Obviously with such a presumed low rate for this

complication, one would need a much larger powered study to give definitive conclusions with regard to the effect of warfarin.

Subgroup analysis of rhegmatogenous retinal detachments in patients on warfarin, revealed a significantly higher proportion presenting with vitreous haemorrhage. The rate of vitreous haemorrhage as a presenting feature with retinal detachment is unclear. An increased rate associated with warfarin anticoagulation has not been previously demonstrated.

Our post operative follow up data did not include information specifically about recurrent vitreous haemorrhage. However only one patient who presented with vitreous haemorrhage required repeat PPV and this patient was not on warfarin.

Guidelines with regard to anticoagulation in ophthalmic surgery are vague. Within the UK, the Royal College of Ophthalmologists recommend that “for certain glaucoma, vitreoretinal, corneal graft, orbital and oculoplastic procedures the decision to modify anticoagulant therapy will be predicated upon the risk-benefit ratio”³. This is due to mixed reports of associated complications. In ophthalmic anaesthesia, the largest study¹⁴ found no increase in risk of haemorrhage in 76 patients on warfarin undergoing peribulbar or retrobulbar anaesthesia. With ocular adnexal procedures, surgeons tend to stop anticoagulation, especially prior to dacryocystorhinostomy procedures¹⁵. Tuli *et al*¹⁶ has suggested that anticoagulation is a significant risk factor in the occurrence of delayed suprachoroidal haemorrhage after glaucoma filtration procedures. With cataract surgery, most studies have shown no increased risk of haemorrhagic complications in patients taking warfarin^{17, 18}.

For vitreoretinal procedures, attitudes towards anticoagulation have been cautious. 81% of the respondents to our survey of members of the British and Eire Association of Vitreo Retinal Surgeons (BEAVRS) suggested that they would withhold warfarin before vitreoretinal procedures.

Interestingly 29% of these surgeons did not risk stratify their patients before withholding warfarin.

Although our early experience suggested that warfarin may have been associated with haemorrhagic

complications⁹, our impression since has been that the risk of stopping anticoagulation outweighs any risks intra and post operatively.

Recent studies have also suggested this. Fu *et al*¹⁹ had good visual outcomes in 25 patients undergoing Vitreoretinal surgery whilst taking warfarin. Only one highly myopic patient suffered a submacular haemorrhage, which resolved with a final visual acuity of 20/40. 44% of their cohort had an International Normalized Ratio (INR) level of <2.0, leading them to suggest that patients INR should be reduced towards 2.0 to reduce haemorrhagic complications. In this study the INR was mean 2.3 and ranged up to 4.6 without a detectable increase in peri-operative complications. Additionally, 73.9% of the patients had therapeutic (INR 2-2.49) or high therapeutic (INR >2.5) anticoagulation. Dayani *et al*²⁰ analysed 54 patients who underwent pars plana vitrectomies or silicone oil removal whilst taking warfarin. They subdivided their patients into sub therapeutic (INR range 1.2-1.49), borderline (INR 1.5-1.99), therapeutic (INR 2.0-2.49) or high therapeutic (INR 2.5 or higher). They experienced no intraoperative haemorrhagic complications. Four patients with INRs of 1.28, 1.41 (sub therapeutic), 2.68 and 2.69 (high therapeutic) suffered post operative vitreous haemorrhage, all these resolved spontaneously requiring no further surgery. They advised that patients may safely undergo vitreoretinal surgery while maintaining therapeutic levels of warfarin anticoagulation.

In conclusion, this is the largest case controlled study of pars plana vitrectomy in patients taking warfarin. A significantly higher proportion of patients taking warfarin presented with vitreous haemorrhage in association with retinal detachment than controls. There was no increase in peri-operative or post operative complications, in particular haemorrhage, in patients taking warfarin. It is our belief that the risks of stopping warfarin anticoagulation are greater than the perceived benefits of reduced complications. We do not recommend that surgeons withhold warfarin treatment before vitrectomy.

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