Is It Really Safe to Discontinue Anticoagulant/antiplatelet Treatment Before Ptosis Surgery From Serious Bleeding?

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Research Article

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Abstract

Purpose

To evaluate the effects of discontinuing anticoagulants (ACs)/antiplatelets (APs) preoperatively on surgery for blepharoptosis

Method

A retrospective analysis included patients with acquired blepharoptosis who underwent surgical correction, and were followed for more than one month. Patients were classified into two groups depending on AC/AP treatment or otherwise. All patients taking AC/AP discontinued with the treatment one week prior to surgery in accordance with our clinical guidelines. Preoperative and postoperative marginal reflex distance 1 (MRD1) and ecchymosis grade were evaluated and compared.

Results

Group 1 (AC/AP treatment cessation) included 47 patients with 93 eyelids, and group 2 (control) included 51 patients with 98 eyelids. The preoperative MRD1 showed no significant difference between groups. Group 1 showed a significantly higher rate of severe ecchymosis (41.8 vs. 22.4%, \( p = 0.004 \)) at 1 week of surgery as well as ‘persistent ecchymosis (58.8 vs. 7.3%, \( p=0.000 \)) compared with group 2 postoperatively at 1 month. Postoperative MRD1 was significantly lower in group 1 at 1 week (\( p=0.019 \)). However, the MRD1 and degree of improvement in lid height (postoperative MRD1–preoperative MRD1) was not significantly different between the two groups (\( p = 0.499 \), \( p = 0.058 \)) at 1 month postoperatively.

Conclusion

Postoperative ecchymosis was more severe in group 1 at one month after ptosis surgery even though the ACs/APs were discontinued. Surgeons should be careful about this before operation.

Introduction

Blepharoptosis is a clinical condition characterized by drooping of one or both eyelids, which affects both the function and appearance of the eyes\[1, 2\]. The surgical correction of blepharoptosis is difficult in that both functional and cosmetic aspects need to be considered. In addition, complications such as ecchymosis and edema, which may appear after ptosis surgery, are not easily predictable, which is a serious clinical concern. Also, ecchymosis and edema complicate the evaluation of potential over- or under-correction after surgery. Therefore, clinicians try to avoid ecchymosis and edema as much as possible, but studies investigating ecchymosis and edema after surgery are scarce.

Along with increased life expectancy and interest in cardiovascular disease, the use of ACs/APs has increased more than ever. AC/AP treatment, especially before surgery, increases the risk of bleeding during surgery\[3, 4\]. Therefore, clinicians recommend discontinuing the use of ACs/APs based on
cardiologist consultation before surgery. However, whether discontinuing the use of ACs/APs has a positive effect on postoperative complications and the outcome of surgery has yet to be investigated. Therefore, our clinical study evaluated the surgical effects of discontinuing ACs/APs preoperatively in patients with blepharoptosis to identify factors associated with outcomes.

**Methods**

This is a retrospective study of patients with acquired blepharoptosis who underwent surgical correction at the Department of Ophthalmology of Dongguk University Ilsan Hospital from January 2014 to January 2020. The study was approved by the Institutional Review Board of Dongguk University, Ilsan Hospital, Goyang, South Korea (Approval number, DUIH 2020-09-009), and adhered to the tenets of the Declaration of Helsinki. The informed consent required was waived because of the retrospective nature and the minimal risk of this study.

In addition to reviewing medical records, the study included 152 patients who were diagnosed with blepharoptosis and underwent surgical correction. All patients received ophthalmologic evaluation for preoperative marginal reflex distance1 (MRD1) and laboratory evaluation to exclude abnormal hematological findings. Group 1 was defined as the group that discontinuing ACs/APs before surgery, and the group 2 was defined as the group that had no history of treatment with ACs/APs. In group 1, the duration, type, and the number of ACs/APs used were investigated for all patients. In current study, AC/AP included all antithrombotic agents such as aspirin, warfarin, clopidogrel, and dabigatran.

Patients who were diagnosed with blepharoptosis involving one or both eyelids and with no hematological abnormalities were included in this study. Patients who were treated with ACs/APs were included only if their discontinuation was recommended by a cardiologist. Patients who failed to discontinue with ACs/APs due to the risk of thromboembolic events, or who did not voluntarily discontinue were excluded. According to the clinical guideline, all patients in group 1 were educated to restart taking ACs/APs 48 hours after surgery.

Surgical correction of blepharoptosis was performed by one surgeon (M.C.). All surgeries were performed under local anesthesia. Preoperative and postoperative MRD1 at one week and one month were calculated automatically using FIJI software (an expanded version of ImageJ version 1.51a, available at fiji.sc, free of charge). The degree of postoperative ecchymosis was evaluated according to Chang M. et al. classification. Ecchymosis grades 0 and 1 were classified as ‘mild ecchymosis, and grades 2 and 3 were categorized under ‘severe ecchymosis’. ‘Persistent ecchymosis’ was defined by the presence of ecchymosis 1 month after surgery regardless of grade. We compared the rate of ‘severe ecchymosis’ between the two groups at 1 week and 1 month postoperatively, and the rate of ‘persistent ecchymosis’ depending on the presence or absence of ecchymosis.

All statistical analysis was performed using IBM SPSS version 21.0 for Windows (SPSS Inc., Chicago. IL, USA).
Independent two-sample t-tests were used to compare normally distributed variables to determine the effect of discontinuing anticoagulant treatment on the degree of ecchymosis and surgical outcomes. Chi $\chi^2$ tests were used to analyze categorical variables. A value of $p<0.05$ was considered as statistically significant difference.

**Results**

The study analyzed 144 patients finally after excluding 8 patients. 3 patients with abnormal platelet counts or coagulation test results and 5 patients who were unable to stop taking AC/AP due to high risk of cardiovascular events were excluded. Group 1 (discontinuing anticoagulants) included 47 patients with 93 eyelids, and group 2 (control) included 51 patients with 98 eyelids. The mean duration of anticoagulant therapy (DOT) in group 1 was 88 months, ranging from 6 months to 120 months. Additional demographics of enrolled patients are shown in Table 1. The prevalence of hypertension was significantly higher in group 1 ($p=0.024$). No major bleeding events such as retrobulbar hemorrhage occurred in either group. Table 2 shows the intergroup comparison of pre- and postoperative MRD1 and the degree of ecchymosis. Preoperative MRD1 showed no significant difference between the groups.

Group 1 (41.8%) manifested a significantly higher rate of severe ecchymosis than group 2 (22.4%) at 1 week post-surgery ($p = 0.004$). Neither group had ecchymosis of grade 2 or higher at 1 month postoperatively. However, Group 1 (58.8%) had a higher rate of 'persistent ecchymosis' than group 2 (7.3%, $p = 0.000$). Postoperative MRD1 was significantly lower in group 1 during the week 1 ($p = 0.019$). However, the MRD1 and the degree of improvement in lid height (postoperative MRD1–preoperative MRD1) was not significantly different between the two groups ($p = 0.499$, $p = 0.058$) at postoperative 1 month. In both groups, under-correction was confirmed one month after surgery in 2 patients with 4 eyelids.

**Discussion**

Oculoplastic surgeons face a dilemma whether or not to discontinue ACs/APs before ptosis surgery. Based on consultation with a cardiologist, most oculoplastic clinicians recommend discontinuing ACs/APs prior to ptosis surgery, but the effect on postoperative outcomes is still unknown.

Previous studies investigated the risk of AC/AP treatment on ophthalmic surgery, but a majority of them analyzed cataract or retinal surgery, with limited focus on oculoplastic surgery. Furthermore, the effect of AC/AP on oculoplastic procedures is still controversial, and there is no valid guideline.

Recent studies revealed that AC/AP treatment has no significant effect in most oculoplastic surgery[5-8]. Bartley reported no major bleeding complication in patients treated with ACs/APs who underwent oculoplastic procedures, including blepharoplasty and dacryocystorhinostomy (DCR) [8]. The American College of Chest Physicians (ACCP) classified eye surgery including oculoplastic procedure as ‘low risk’, which is defined by a probability of 0 to 2% of major bleeding events occurring within 2 days of surgery.
and recommended continuing treatment with AC/AP perioperatively [9]. Similarly, our previous study revealed that the use of intraoperative ketorolac, known as blood thinner, in oculoplastic surgery does not increase postoperative bleeding risk [10]. Other studies also revealed the low incidence of severe complications in patients undergoing anticoagulant therapy and non-significant differences compared with control group. Philip et al. analyzed the intraoperative and postoperative complications in patients undergoing oculoplastic procedure, and reported that the proportion of major complications affecting the surgical outcome was only 0.4% and found no statistically significant difference among patients with and without taking AC/AP [6]. As new anticoagulants, including direct oral anticoagulant (DOAC), previously known as new oral anticoagulants (NOAC), are routinely recommended, several studies have investigated the half-lives of DOACs. A study published in the *European Heart Journal* showed that DOACs have comparable half-lives and suggested that their residual anticoagulant effects do not differ or persist upon treatment interruption [11].

However, our results were inconsistent with their results, and confirmed the effect of ACs/APs. Interestingly, our study showed significant ecchymosis and edema after surgery despite adequate discontinuation of ACs/APs. The degree of postoperative ecchymosis was severe in the group that discontinued with ACs/APs before surgery at postoperative one week and one month despite proper discontinuation. In addition, postoperative MRD1 was significantly lower in group 1 at one week.

Similarly, traditionally even if ACs/APs are discontinued appropriately prior to oculoplastic surgery, the risk of severe complications such as retrobulbar hemorrhage may still remain. According to questionnaire surveys, the majority of oculoplastic surgeons experienced various intraoperative or postoperative complications in patients with a history of ACs/APs usage [12]. Parkin et al argued the risks of taking anticoagulants prior to blepharoplasty, indicating that the incidence of ocular hemorrhage was high in patients who took ACs/APs [13].

While these contrasting studies have focused on intraoperative and postoperative complications in patients taking ACs/APs, the effects of such complications on surgical outcomes were unclear. Furthermore, especially in patients undergoing blepharoplasty, it is necessary to focus on more common complications such as postoperative ecchymosis, edema or under-correction rather than major complications such as retrobulbar hemorrhage. Therefore, the aim of our study was to determine the effect of discontinue anticoagulant use before surgery on the degree of ecchymosis after surgery and the effect on the surgical outcome.

The possible mechanisms supporting our findings are as follows. First, irreversible hematologic or microvascular changes may have occurred due to hypertension and long-term use of ACs/APs. Wall et al [14] reported that hypertension was a predictor of permanent vascular change. In our study, the prevalence of hypertension was significantly higher in the group exposed to ACs/APs, which may have altered the postoperative outcome. Second, the action of ACs/APs would have persisted even when the anticoagulant was discontinued. Two studies [15, 16] reported residual serum concentrations of ACs/APs in patients who underwent elective invasive procedures. Anne et al [15] confirmed persistent
anticoagulant effects in most patients even after discontinuing for 3 times the half-life of the known anticoagulant. Another possible hypothesis is that delayed bleeding occurred due to re-administration of ACs/APs after surgery. In fact, the challenge of delayed bleeding after endoscopy-like procedures in patients taking ACs/APs is being debated worldwide. Hideomi et al. [17] argued the possible risk of delayed bleeding in patients taking ACs/APs. Harada et al. [18] also reported a 9% higher rate of delayed bleeding. Similarly, our study confirmed that the clinical application of the currently known half-lives of ACs/APs in periprocedural management is unstable. Therefore, in line with the emergence of new ACs/APs and their increased use, further active studies investigating periprocedural management are needed.

Unfortunately, our study has some limitations that have yet to be clearly addressed. First, this study was retrospective with a relatively small sample size, which may limit the statistical power. Second, no objective indicators were available to quantitatively evaluate the degree of bleeding experienced by patients. In addition, the ecchymosis grade and persistence can be proxy and subjective despite evaluation by 4 masked graders to minimize bias. Lastly, we could not compare and analyze the effects of ACs and APs respectively, as most patients took dual or combined administration. It is thought that further studies on the individual effects of each drug are needed in the future.

Otherwise, it is important to balance the risk of potential intraoperative bleeding and postoperative ecchymosis against the risk of systemic thromboembolic events. Therefore, the oculoplastic surgeon must establish proper guidelines for patients taking and discontinuing ACs/APs by evaluating the possible complications and surgical outcomes. Also, the possible complications after surgery need to be borne in mind, even if the drugs are discontinued properly. Fortunately, the patients should be reassured and monitored during the intervention and subsequently. Even if such ecchymoses and edema occur, there may be no significant effects on the surgical outcome.

In conclusion, postoperative ecchymoses were more severe in group 1 by one month after ptosis surgery even though after discontinuing with ACs/APs. Surgeons should be careful about this before operation.

Declarations

Acknowledgements

Not applicable.

Author’s contribution

KML, CYP and MWC were responsible for the conception and design for this study. KML, CYP AND MWC acquired and analyzed the data. KML, CYP AND MWC wrote the draft and revised the manuscript critically. All authors have read and approved the final manuscript.

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Availability of data and materials

All data are available upon request to the corresponding author at mdjacob76@gmail.com.

Declarations

Ethics approval and consent to participate

This study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Dongguk University, Ilsan Hospital, Goyang, South Korea (IRB no. 2020-09-009).

Consent for publication

Not applicable (no identifying patient data). The informed consent required was waived because of the retrospective nature and the minimal risk of this study

Competing interests

The authors declare that they have no competing interests except that the author, Choul Yong Park, serves as a member of editorial board of BMC Ophthalmology

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Tables

Table 1. Demographics of patients discontinuing ACs/APs vs. control group.

| Characteristics               | Group 1 (n = 47) | Control (n = 51) | p-value |
|-------------------------------|------------------|------------------|---------|
| Number of eyelids             | 93 (48.7%)       | 98 (51.3%)       |         |
| Age, years                    | 69.9 ± 8.2       | 68.8 ± 8.8       | 0.528   |
| Male, n (%)                   | 18 (38.3%)       | 23 (45.1%)       | 0.495   |
| Duration of treatment (DOT), months | 88               |                  |         |
| Baseline comorbidities        |                  |                  |         |
| Hypertension                  | 31 (66.0%)       | 22 (43.1%)       | 0.024   |
| Diabetes                      | 19 (40.4%)       | 13 (25.5%)       | 0.115   |

P values were calculated with t-test, chi square test

Table 2. Comparison of subjects’ preoperative and postoperative outcomes.
| Characteristics                             | Group 1 (n = 47, 93 eyelids) | Control (n = 51, 98 eyelids) | p-value |
|--------------------------------------------|------------------------------|------------------------------|---------|
| MRD1                                       |                              |                              |         |
| Preoperative                               | 0.84±1.10                    | 1.30±1.30                    | 0.066   |
| One week                                   | 2.56±0.85                    | 2.84±0.79                    | 0.019   |
| One month                                  | 2.98±0.93                    | 3.07±0.84                    | 0.499   |
| Ecchymosis grade                           |                              |                              |         |
| Severe ecchymosis (1 week, %)              | 41.8%                        | 22.4%                        | 0.004   |
| Persistent ecchymosis (1 month, %)         | 58.8%                        | 7.3%                         | 0.000   |
| Improvement in lid height (mm)             |                              |                              |         |
| One week                                   | 1.71                         | 1.56                         | 0.371   |
| One month                                  | 2.14                         | 1.78                         | 0.058   |
| Under-correction at one month              | 2 (4 eyelids)                | 2 (4 eyelids)                |         |

**MRD1** = marginal reflex distance 1

**P values were calculated with t-test, chi square test**