Eye Surgery and Anticoagulation

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Management of antithrombotic therapy: studies often limited by sample size, retrospective nature, and lack of controls; type and dose of antithrombotics not standardized; risk for bleeding varies with type of eye surgery; forming conclusions difficult because event rates low; risk for bleeding must be balanced against risk for thromboembolism; consider indications for therapy, timing of thrombotic event, type of antithrombotic, past ocular history and operations, and type of surgery; surgical techniques can decrease risk for bleeding

Risk for thromboembolism: low — atrial fibrillation with low CHA2DS2-VASc score (congestive heart failure, hypertension, age ≥75 yr, diabetes, history of stroke, vascular disease, sex) and thrombotic disease ≥1 yr ago; therapy may be discontinued; high — high CHA2DS2-VASc score; thromboembolism within past 3 mo; acute coronary syndrome; recent cardiac stenting; serious thrombophilia; antithrombotic therapy should continue

Surgical procedures: anterior eye chamber — considered low risk; surgery controllable, not excessive, and causes no damage to eye; posterior chamber — usually considered high risk; associated retrobulbar bleeding can affect vision

Discontinuation of antithrombotics: antiplatelet therapy — may result in major cardiovascular events, thrombosis of cardiac stents, myocardial infarction (MI), stroke, or death; anticoagulants — may result in valvular heart disease, thrombosis of valves, pulmonary embolism, stroke, or death; antiplatelet therapy after stenting — rate of stent thrombosis 10%; risk for death or major adverse cardiac event 30%; clopidogrel (Plavix) <3 mo after acute coronary syndrome — risk for major adverse cardiac event 10%; aspirin for secondary prophylaxis — risk for stroke increases by 40%; warfarin for mechanical heart valve — risk for embolism increases 4-fold

Newer anticoagulants: dabigatran, rivaroxaban, and apixaban; exhibit direct action on factor II or X; given as daily fixed dose; no antidote available; requires no testing of International Normalized Ratio (INR); onset rapid (1-3 hr, vs days for warfarin); short half-life (10-15 hr) important consideration when discontinuing therapy before surgery; observational studies — spontaneous bleeding rates 1% to 1.5% (similar to those with warfarin; time between discontinuation and surgery — 3 half-lives recommended (30-51 hr); 5 days if patient on dabigatran, has renal failure, creatinine clearance <50 mL/min, or elderly; rapid drug action may necessitate waiting 24 hr after surgery before restarting; perioperative management — because data lacking, recommendations based on pharmacology and bleeding risk; longer period of discontinuation required if patient has renal or hepatic disease; bridging therapy possibly necessary; emergency surgery — attempt to delay for 2 half-lives; clotting factors — administer if bleeding occurs; patients with high bleeding or thromboembolic risk — discontinue 5 days before surgery; bridge with low-molecular-weight heparin (discontinue 24 hr before surgery); restart anticoagulant on postoperative day 1 or 2

Antiplatelet therapy: mainstay treatment for many cardiovascular and thromboembolic diseases; different drugs have different receptors, onset of action, and recovery time; aspirin — irreversible platelet inhibitor; half-life short; platelets usually recover at rate of 10% to 15%/day; discontinuation 3 to 5 days before surgery recommended (>50% of platelet function must be recovered)

ADP receptor antagonists: ticlopidine, clopidogrel, prasugrel, and ticagrelor; ticagrelor only reversible oral antithrombotic agent; cangrelor — awaiting approval; action similar to that of clopidogrel; given intravenously (IV); time to recovery minutes to 1 hr; prasugrel and ticagrelor — cause more rapid and potent inhibition of platelet aggregation than clopidogrel; ticagrelor associated with increased risk for dyspnea and bradycardias; prasugrel must be discontinued 7 days before surgery to allow platelet recovery; prasugrel superior for prevention of stroke and acute coronary syndromes, but increases risk for bleeding

Dual antiplatelet therapy: usually prescribed after acute coronary syndrome; increases risk for surgical bleeding; postpone elective surgery until patient beyond period of high risk for thromboembolism, then discontinue one drug; for urgent procedures, both drugs may be continued, or one or both drugs may be stopped, depending on bleeding risk (make decision in conjunction with cardiologist); resume therapy as soon as feasible; if possible, perform procedure in hospital with availability of interventional cardiology

Perioperative management: continue medication if risk for bleeding low; discontinue prasugrel or ticagrelor if risk moderate to high; use bridging agent if thrombotic risk high

Ophthalmic anesthesia: by 2003, 95% of procedures performed under local anesthesia; incidence of eyelid hemorrhage 2% to 4%; retrobulbar bleed — risk 0.001% to 1%; arterial fragility (due to hypertension or diabetes) main risk factor; risk

Educational Objectives

The goal of this program is to improve outcomes of patients undergoing eye surgery and management of hyperthermia. After hearing and assimilating this program, the clinician will be better able to:

1. Assess the safety of antithrombotic therapy in patients undergoing eye surgery.
2. Evaluate the evidence on the risk for bleeding associated with antithrombotic therapy and ophthalmologic analgesia.
3. Cite benefits and risks of the newer antithrombotic agents.
4. Distinguish malignant hyperthermia from conditions with similar presentations.
5. Prevent and manage malignant hyperthermia in the ambulatory surgery setting.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing to disclose.
minimized by use of single-injection techniques, shorter and finer needles, and injecting through poorer vascular compartments; incidence of vision-threatening hemorrhage associated with peribulbar or retrobulbar anesthesia generally low, even when nonsteroidal anti-inflammatory agents (NSAIDS) continued; increase in grade 1 (spot ecchymosis of eyelid; conjunctival hemorrhage) and grade 2 (eyelid ecchymosis over one-half of eyelid surface) seen with use of antithrombotics, with no sequelae; grades 3 and 4 rare

Ophthalmic analgesia studies: aspirin — most studies show no significant increase in retrobulbar bleeding with orbital blocks in patients on antiplatelet therapy; clopidogrel — cataract study (Benzimra) found increase in mild to moderate bleeding; studies of vitrectomy show no increase in risk for retrobulbar bleed; Kallio study — concluded that limiting aspirin or NSAIDS unnecessary before orbital blocks; warfarin — 2 studies show no association with increased bleeding; in Benzimra study, risk for needle bleeding increased by 3% (therapeutic INR associated with lower risk for bleeding); combination of aspirin and warfarin associated with ≤6.5% increase in subconjunctival hemorrhage; ≥70% of ophthalmologists continue antithrombotic agents when performing surgery, usually without increase in serious ocular bleeding; however, some procedures carry higher rates of bleeding; no consensus reached on whether risk greater with antiplatelet therapy or anticoagulants

Ophthalmic Surgery

Bleeding complications: ecchymosis of eyelid; retrobulbar hemorrhage; hyphema; suprachoroidal hemorrhage — most serious but rare; usually causes loss of vision; most often associated with cataract surgery; risk factors include advanced age, arteriosclerosis, diabetes, hypertension, glaucoma, myopia, and recent surgery; not usually associated with anticoagulant or antiplatelet agents alone

Cataracts: avascular procedure; usually performed under topical or intracameral anesthesia; maintenance of antiplatelet or anticoagulant therapy generally does not increase risk for severe bleeding or ophthalmic complications; meta-analysis — rate of hyphema 10% in patients taking warfarin; bleeding self-limited and insignificant

Vitrectomies: rate of bleeding complications (mild to severe) 12%; most studies show no increase in serious complications in patients taking warfarin; Chandra study — risks of discontinuing warfarin greater than risk for bleeding; Ryan study — concluded antithrombotics can be safely continued in most patients; rate of bleeding with combination of aspirin and clopidogrel slightly higher than with aspirin alone

Oculoplastics: highly vascular, so incidence of bleeding (0.05% to 0.4%) slightly higher; Haas study — for cosmetic eye surgery, risk for bleeding 1 in 2000, and risk for visual loss 1 in 10,000; Custer study — rates similar with and without continuation of antithrombotics; Kent study — continuation of anticoagulant therapy possibly appropriate in patients at high risk for vascular events, with attention to maintenance of adequate hemostasis

New oral anticoagulants (apixaban, dabigatran): no clinical data available on safety in most ophthalmic surgeries; at least as effective as warfarin

Malignant Hyperthermia

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Hyperthermia: increased metabolic rate, sympathetic activity, and hormonal effects; muscle hypertonicity; seizures; shivering; has multiple causes; pediatric hyperthermia — causes include warm environment, iatrogenesis, hypovolemia, allergy, anticholinergic medications, thyrotoxicosis, pheochromocytoma, pediatric stroke, blood in central nervous system; neonates — iatrogenesis most common cause of hyperthermia; neonatal sepsis causes hyperthermia; rare causes of hyperthermia include status epilepticus (in asphyxiated brain), typhoid, hepatitis B vaccination, and congenital brain malformations

Primary central nervous system: ≥50% of patients develop fever within 72 hr of bleeding into brain; standard antipyretics not useful in stroke because blood-brain barrier no longer intact; priapism disease — can cause temperature elevation; central thermoregulatory failure — very rare

Toxic exposures: eg, aspirin toxicity, phenycyclidine poisoning; treatment hemodialysis and alkalization; dantrolene not appropriate; bactofen withdrawal — may cause critically elevated blood pressure; aggressive dantrolene therapy appropriate pending restart of bactofen; dantrolene possibly effective for methylenedioxy-methamphetamine (MDMA), cocaine, and monoamine oxidase inhibitors; however, carvedilol and benzodiazepines treatment of choice; do not use standard therapy (prognosis dismal if temperature reaches 44°C); sedatives and physostigmine treatments of choice for anticholinergic fever; serotonin syndrome usually caused by combination drug therapy

Withdrawal: alcohol — benzodiazepines and supportive care best treatment; opioids and benzodiazepines — efficacy of dantrolene unknown, but dexametomidine highly effective

Infection: envenomation does not cause hyperthermia (but resulting localized infection can increase temperature); dantrolene — effectiveness in bacterial sepsis reported anecdotally; not specific for malignant hyperthermia (MH) or spasticity; not optional for malaria or West Nile virus

Heat-related illness: heat stroke — requires immediate treatment; dantrolene may be useful if temperature highly elevated, but surface cooling and other active treatments also helpful; exertional heat-related illness and rhabdomyolysis — patients do not have altered level of consciousness; pathology similar to heat stroke; however, exertional heat illness and MH strongly related; administer dantrolene and rehydrate

Conditions associated with MH: King-Denborough syndrome; carnitine palmitoyltransferase (CPT) II deficiency; central core disease (only cause of spontaneous awake MH)

Erroneous associations in literature: Noonan syndrome; osteogenesis imperfecta; arthrogryposis; idiopathic hyper-CK-emia; Duchenne muscular dystrophy; Becker muscular dystrophy; endocrinopathies (including MH-like syndrome seen in obese black men, thyroid storm, and evacuation of molar pregnancy [human chorionic gonadotropin β subunit similar to thyrotropin]; dantrolene indicated if hyperthermia severe); pheochromocytoma; neuroleptic malignant syndrome (usually self-limited; dantrolene possibly effective; bromocriptine best treatment)

MH in the Ambulatory Environment

Incidence of MH: NY study — 0.3 per 100,000 in ambulatory surgery centers (ASC); does not occur unless triggering agents used; patients at risk for MH not treated in ASC often because of significant comorbidities, unprepared facility and practitioners, and other fears and concerns

Treating patients with susceptibility to MH: use nontriggering agents, regional anesthesia, and provide low-stress environment; preparation — existing transfer agreement with local hospital recommended; cart contents — standardized for office or ASC; procainamide and manitol no longer used; dantrolene
in ASC study — concluded that stocking dantrolene for treatment of MH in ASCs cost-effective when expense compared to value of life per insurance company estimates (ie, $3 million); true incidence of MH uncertain; however, fatality rate of MH 80% to 90% before dantrolene used (currently 10%-20%); general anesthesia acceptable for MH-susceptible patients in free-standing ASC if anesthesia machine properly prepared and appropriate (ie, total IV) anesthetic used; monitor temperature (however, no current standard recommends monitoring of temperature); preparation of machine — remove vaporizer, change CO₂ absorbent, flush lines, and add new circuit; charcoal filter can be used on inspiratory and expiratory limbs (effectively removes levels of triggering volatile anesthetic to <5 ppm).

**Protocol for MH in ACS:** Begin treatment; call MH hotline and for emergency assistance (911); discontinue any triggering agents; administer dantrolene before transport, if possible, but do not delay transport to administer; transfer while continuing treatment; accompany patient to hospital (to, eg, protect IV access); ensure receiving institution capable of handling patients with MH; place urinary catheter; consider sending patient by ground, air, or both; send dantrolene with patient if anesthesia provider unable to accompany; uneventful ASC procedures on MH-susceptible patients — keep in postanesthesia care unit for ≈1.5 hr afterward.

**Additional notes:** Succinylcholine alone capable of triggering MH (dantrolene must be available); MH-susceptible anesthesia providers — able to provide care (trace amounts do not trigger MH); men more likely to be triggered than women.

**Questions and answers:** Temperature monitoring in MH — increased temperature late sign, but monitoring still important; early signs depend on age of patient; mixing dantrolene — use warmed water; new formulation clear in solution while injecting; strabismus and MH — speaker doubts relationship exists (looks for other signs of potential for MH).

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**Suggested Reading**


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1. Which of the following characteristics are associated with newer anticoagulants (dabigatran, rivaroxiban, and apixaban)?

1. Longer half-life, compared with warfarin
2. Direct action on clotting factors
3. Required testing of International Normalized Ratio
4. Rapid onset of action
5. Fixed daily dose

(A) 1,2 (B) 3,4 (C) 1,3,5 (D) 2,4,5 **

2. Platelet recovery after discontinuation of antiplatelet therapy before surgery is deemed sufficient when _______; _______ is a reversible oral antiplatelet agent.

(A) >50% of platelet function has been restored; ticagrelor
(B) 7 to 10 days have elapsed; ticagrelor
(C) >50% of platelet function has been restored; clopidogrel
(D) 7 to 10 days have elapsed; clopidogrel

3. Which of the following statements about the risk for bleeding associated with ophthalmic anesthesia is true?

(A) There are no specific surgical techniques that minimize risk
(B) Arterial fragility is the main risk factor for retrobulbar bleeding
(C) The risk for peribulbar or retrobulbar bleed due to ophthalmic analgesia is ≈5%
(D) The risk for eyelid hemorrhage is 10% to 15%

4. All the following are associated with suprachoroidal hemorrhage, except:

(A) Cataract surgery (C) Use of antithrombotic agents alone **
(B) Advanced age (D) Loss of vision

5. Studies of patients treated with antithrombotic therapy who underwent glaucoma surgery suggest which of the following?

(A) Most surgeons discontinue anticoagulation before glaucoma surgery
(B) Warfarin is not associated with an increased risk for bleeding
(C) Antiplatelet agents increase the risk for hemorrhagic complications in glaucoma surgery **
(D) Robust data are available for guiding decisions on whether to discontinue or maintain therapy

6. The most common cause of hyperthermia in neonates is:

(A) Iatrogenesis ** (C) Hepatitis B vaccination
(B) Sepsis (D) Typhoid

7. The treatment regimen of choice for patients with hyperthermia due to monoamine oxidase inhibitors, cocaine, or methylenedioxymethamphetamine (MDMA) includes which of the following?

(A) Dantrolene (C) Physostigmine
(B) Standard antipyretics (D) Carvedilol

8. Patients with exertional heat-related illness and rhabdomyolysis _______ develop altered level of consciousness; treatment with dantrolene _______ appropriate.

(A) Often; is (C) Often; is not
(B) Do not; is **(D) Do not; is not

9. Which of the following is not recommended for treating patients susceptible to malignant hyperthermia (MH) in an ambulatory surgery center?

(A) Use of charcoal filters on inspiratory and expiratory limbs of the anesthesia machine
(B) Use of total intravenous anesthesia
(C) Enabling the vaporizer on the anesthesia machine **
(D) Monitoring patient temperature

10. All the following actions are appropriate if a patient develops MH while undergoing treatment in an ambulatory surgery center, except:

(A) Discontinue any triggering agents, and begin treatment
(B) Call the MH hotline and emergency medical services
(C) Delay transport until dantrolene administered **
(D) Accompany the patient to hospital, or send dantrolene with the patient

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