Chapter 44

Ocular Patients

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General Considerations

Development of an appropriate anesthetic protocol for any ocular patient should include not only drug selection, but also a perioperative management plan to provide an optimal postoperative outcome. This requires knowledge of not only the patient's physical status and the ophthalmic procedure to be performed, but also familiarity with ocular physiology and current medications administered for ophthalmic purposes.

Ocular and periocular structures are often neglected during anesthesia induction. Positioning of hands and equipment relative to the eyes should be noted during induction, especially when dealing with severely compromised globes with the potential to rupture. Mask induction may not be an option if the mask rubs or presses on the eye, and a patient's struggling during induction with a face mask may increase intraocular pressure (IOP) or potentiate eye rupture. Similarly, nasotracheal intubation in awake foals requires heavy restraint and is accompanied by coughing and gagging, which may increase IOP and further compromise the globe. Providing analgesia is particularly important in ophthalmic patients with substantial discomfort from their primary ophthalmic disease. These patients may be more inclined to struggle when restrained, which may result in increased IOP and additional damage to the globe during induction.

Horses with a nonvisual eye should be approached from the visual side. If approach from the nonvisual side is necessary, it should be accompanied by words of reassurance and gentle hand contact, which should be maintained until induction is complete. Movement of equine patients to lateral recumbency after induction should include careful control of the head to prevent additional trauma to the eyes. It has been suggested that ventral positioning of the head relative to the body during transport causes venous stasis and increased IOP. These effects may be responsible for intraocular hemorrhage observed shortly after induction in horses with traumatized eyes.[1] Supporting the head to keep it level with the body is recommended to avoid such an occurrence.

Protection of the dependent, nonaffected eye should also be considered during positioning of patients. Corneal protection of the eye not operated on in unilateral procedures may be afforded by application of corneal lubrication with or without a temporary tarsorrhaphy. Positioning of the patient's head and application of any topical ophthalmic preparations should be coordinated between the anesthesiology personnel and ophthalmologist to ensure the best possible surgical outcome when both eyes are to be operated on. Collapse of the anterior chamber of the dependent eye, possibly resulting from increased aqueous outflow caused by physical pressure on the globe, has been reported in birds positioned in lateral recumbency. The anterior chamber was reestablished within a few minutes of repositioning.[2] Resting the periocular region of the dependent eye on a soft padded eye ring or "doughnut" may help protect the eye from corneal abrasion and external globe compression that may result in hypotony.

Laryngeal stimulation should be minimized and endotracheal intubation accomplished as smoothly as possible to avoid any possible increases in IOP.[1] Lidocaine applied topically to the larynx, or administered intravenously (1.0 mg/kg), may be helpful in suppressing the cough reflex.[3] In people, the anesthesia-related practices most likely to increase IOP significantly (i.e., at least 10 to 20 mm Hg) are laryngoscopy and endotracheal intubation.[4–6] Although the mechanism is not clear, it has been suggested that it is related to sympathetic cardiovascular responses to laryngeal stimulation. The occurrence of increases in IOP during endotracheal intubation has not been clearly established in veterinary patients.

Positioning for the ophthalmic procedure may render ocular patients less accessible for anesthetic monitoring, and maintaining their appropriate level of anesthesia may become very difficult. Eye reflexes, jaw tone, and oral mucous membranes will not be assessable, although the ophthalmologist may be able to provide information about eye position and movements. Once the

head has been surgically draped, the airway also becomes inaccessible. A guarded (i.e., wire reinforced) endotracheal tube is recommended to prevent unobservable kinking and occlusion of the airway during surgical positioning. Capnography may be useful for detection of an obstructed airway or inadvertent disconnection from the anesthetic delivery system. Similarly, pulse oximetry may help detect desaturation should the endotracheal tube become kinked or the delivery system disconnected. However, the pulse oximeter may have to be placed somewhere other than on the tongue, which would put it in close proximity to the surgical field, where movement by the ophthalmologist may interfere with its function.

Monitoring heart rate (HR) and arterial blood pressure (BP) becomes essential in ocular patients when other types of monitoring are limited and are particularly important when including neuromuscular blocking agents (NMBs) in the anesthetic protocol. Preventing movement during ophthalmic procedures and facilitation of eye positioning may be accomplished by using NMBs to paralyze patients, but the inability of patients to indicate inadequate anesthesia with movement makes monitoring all the more crucial. Increased BP or HR may indicate an inadequate plane of anesthesia or the need for additional analgesics. Conversely, precipitous decreases in HR or BP may indicate too deep a plane of anesthesia or initiation of the oculocardiac reflex (OCR). Increased respiration rate may also be indicative of inadequate anesthesia, but such a response may not be evident in mechanically ventilated or paralyzed patients.

Tear production decreases during general anesthesia in people, dogs, horses, and possibly other species.[7–10] Tear production in dogs decreases from baseline values within 10 to 15 min after subcutaneous administration of atropine and continues to decline after induction of general anesthesia with halothane or methoxyflurane. Indeed, within 30 to 60 min of onset of general anesthesia, tear production in dogs can approach negligible amounts regardless of whether atropine was administered before surgery. In a comparison of preanesthetic and postanesthetic Schirmer tear test values in dogs, significant decreases in tear production were evident for up to 24 h after the anesthetic procedure. Anticholinergic administration before or during anesthesia further decreased the postanesthetic Schirmer tear test values.[11] Based on drug-retention studies in humans, it has been suggested that canine eyes be lubricated every 90 min during general anesthesia.[7] A study comparing the effects of sedative and opioid combinations on tear production in dogs determined that acepromazine-oxymorphone, diazepam-butorphanol, and xylazine-butorphanol significantly decreased tear production (80%, 68%, and 33% of baseline, respectively).[12] Xylazine alone did not significantly decrease tear production. Butorphanol alone did significantly decrease tear production, but when xylazine and butorphanol were combined, the decrease in tear production was greater than that observed with butorphanol alone. This suggests that xylazine and butorphanol act synergistically to decrease tear production in dogs.

Transient lens opacification may occur in rodents, such as mice, rats, and hamsters, during prolonged sedation or anesthesia. The opacification is believed to be caused by lack of blinking and subsequent evaporation of fluids from the shallow anterior chamber, which then resolves upon awakening.[13]

In horses undergoing general anesthesia, tear production is reduced much less dramatically than in dogs. Normal tear production was restored within 3 h in horses undergoing halothane anesthesia.[9] Although this may suggest that ocular lubrication may not be necessary to prevent corneal drying in horses, it is recommended that ocular lubrication be instilled in the eyes of all patients undergoing anesthesia. A flash fire involving ophthalmic ointment during anesthesia with nitrous oxide and oxygen has been reported,[14] but a later study concluded that ophthalmic ointments do not offer a significant fire hazard.[15] If intraocular surgery is planned or globe rupture has occurred, application of topical ophthalmic medications or lubrication should be restricted to aqueous-based formulations. Petroleum-based ointments that gain access to intraocular structures may cause severe uveitis and further compromise vision and ocular comfort. Taping the palpebrae closed or a partial temporary tarsorrhaphy are additional techniques for protecting the globe and keeping it moist.[1]

A smooth anesthetic recovery, including appropriate analgesia and prevention of self-trauma, is the primary postoperative management goal. For patients who have undergone intraocular surgery, periods of excitement, incoordination, coughing, gagging, or retching are particularly undesirable. Recovery should be in a quiet, dimly lit enclosure where external stimuli will be kept to a minimum. Patients can be kept comfortable and quiet by appropriate analgesia and sedation, although minimal physical restraint or words of reassurance while holding some small patients may be more effective. Elizabethan collars for small patients and padded helmets or protective eyecups for large patients may help protect their eyes, but may not be readily tolerated by some. Recovery cages or stalls should have extraneous structures, such as feed-bowl rings, removed to prevent eye trauma during recovery.

Physiological Considerations

Ocular Physiology

Selection of an anesthetic protocol for intraocular surgery should include consideration of the effects on IOP, pupil size, and globe position.[1]

Intraocular Pressure

Success of an ophthalmic procedure may depend on control of IOP before, during, and after the procedure. The overall effect of most anesthetics is to decrease IOP.[15] This reduction may be attributable to a combination of factors, including depression of diencephalic centers regulating IOP, increased aqueous outflow, decreased venous and arterial BPs, and relaxation of extraocular musculature.[16] Many of the factors affecting IOP are listed in Table 44.1.

IOP is determined by aqueous humor dynamics, intraocular (choroidal) blood volume, central venous pressure, and extraocular muscle tone.[16] Normal range of IOP has been reported for dogs (10 to 26 mm Hg), cats (12 to 32 mm Hg), and horses

Table 44.1. Factors altering intraocular pressure.

Altering Factors	Change in IOP	Comments
Blockade of aqueous outflow	↑	Caused by any position or maneuver that increases CVP
Acute increase in arterial pressure	↑	Causes only a transient increase in IOP
Hypoventilation, airway obstruction, hypercapnia, choroidal vessel dilatation	↑	
Hyperventilation, hypocapnia	↓	
Endotracheal intubation	↑	Topical or IV lidocaine may prevent coughing, gagging, straining
Eyeball pressure	↑	Caused by face mask, orbital tumors, surgical traction, eyeball position, retrobulbar injection
Anesthetic drugs		
Barbiturates	↓	May depress central control of IOP or promote aqueous outflow
Propofol	↓	May prevent intubation-associated increase in IOP; may suppress depolarizing NMB-induced increase in IOP
Etomidate	↑	May be predominantly due to etomidate-induced myoclonus
Ketamine	↑ or ↓	Contradictory; effect may depend on premedication
α_2-Agonists	↓	Induces bradycardia, may promote OCR; may induce vomiting; may suppress sympathetic input and aqueous production
Benzodiazepines	↓	May be in response to central relaxation of ocular muscles
Acepromazine	↓	Decreases arterial blood pressure, suppresses retching and vomiting
Opioids	↓	IOP may increase with opioid-induced vomiting or retching
Neuromuscular blockers		
Depolarizing		
Succinylcholine	↑	Transient increase in IOP
Nondepolarizing	↓	Decrease or no effect
Pancuronium		
Vecuronium		
Atracurium		
Other drugs		
Methazolamide	↓	Carbonic anhydrase inhibitor; decreases formation of aqueous humor
Hypertonic solutions (mannitol)	↓	Increases plasma osmotic pressure, decrease aqueous humor formation
Phenylephrine	↑ or ↓	Effect is dosage dependent
Epinephrine	↑ or ↓	Effect is dosage dependent

CVP, central venous pressure; IOP, intraocular pressure; IV, intravenous; NMB, neuromuscular blocking agent; and OCR, oculocardiac reflex.
Modified from Thurmon et al.,[3] p. 814.

(mean, 23.5 to 28.6 mm Hg).[17–19] For intraocular surgery, a low normal IOP is desirable.[5] Lens or vitreous prolapse, expulsive choroidal hemorrhage, and subsequent retinal detachment are possible sequelae to increased IOP during or after intraocular surgery or in patients with penetrating eye wounds.[5]

Normal IOP depends on the delicate balance between aqueous inflow (production) and aqueous outflow (filtration).[1,16] Obstruction of outflow, which may dramatically increase IOP, may be induced by coughing, retching, vomiting, excessive restraint of the head and neck, or any maneuver or position that increases central venous pressure.[5] Indeed, coughing may increase IOP by as much as 40 mm Hg.[20]

Aqueous humor is produced primarily by the ciliary body. It flows from the posterior chamber anteriorly through the pupil into the anterior chamber. Most of the aqueous humor exits the anterior chamber via the filtration angle of the eye, following a pattern of flow referred to as *conventional outflow*.[1] In conventional outflow, aqueous humor enters the venous vascular system via the scleral venous plexus (analogous to Schlemm's canal in humans), drains into the vortex veins, passes through the orbital vasculature, and ultimately enters the episcleral venous system. The small percentage of aqueous humor that exits the anterior chamber via diffusion through iris stroma and ciliary body musculature is referred to as uveoscleral or *unconventional outflow*. In unconventional outflow, aqueous humor flows caudally to enter the suprachoroidal space and ultimately, the scleral and choroidal vasculature.[1]

Intraocular (choroidal) blood volume is determined by arterial inflow, venous outflow, and tone of the intraocular vasculature.[6] Autoregulation of choroidal blood flow minimizes the effects of arterial BP on choroidal blood volume and IOP. Sudden increases in systolic arterial BP may cause a transient increase in choroidal blood volume and IOP, but a temporary increase in outflow will adjust IOP back to normal. Sudden increases in choroidal blood

volume may also displace the vitreous forward into the anterior chamber during intraocular surgery or in patients with penetrating eye wounds. Marked IOP reductions may occur when systolic arterial pressure decreases below 90 mm Hg and choroidal blood volume decreases.[5]

A more direct, definitive relationship exists between central venous pressure and IOP.[16] Increases in central venous pressure can increase IOP and choroidal blood volume by diminishing aqueous-humor outflow into the venous system.[5] To maintain normal central venous pressure and IOP in humans, a slightly head-up position is preferred for patients undergoing intraocular surgery.[6]

Choroidal blood volume and consequently IOP increase in response to increases in $PaCO_2$ and decreases in PaO_2.[21] Hypercapnia and hypoxemia induce vasodilatation, which increases intraocular blood volume accompanied by an increase in IOP. Conversely, respiratory alkalosis and hyperbaric oxygen conditions induce vasoconstriction and decreased aqueous-humor formation through reduced carbonic anhydrase activity, which decrease choroidal blood volume and IOP.[21] In anesthetized dogs, inspired concentrations of 5% CO_2 caused a mean increase in IOP of 35.2%. Concentrations of 10% to 15% CO_2 increased IOP even higher.[21] There is no apparent correlation between increased $PaCO_2$ and IOP in anesthetized horses.[22] Unlike other species, horses have a greater dependence on unconventional outflow of aqueous humor, which may result in a more constant IOP during hypercapnia.

Vitreous has been described as a hydrogel consisting of a loose fibrillar network of collagen that supports the lens anteriorly and the retina posteriorly.[1] Although the vitreous volume is fairly constant, it may be decreased by administration of hyperosmotic agents, such as mannitol or glycerin. As indicated previously, vitreous may be displaced by changes in intraocular blood volume, but also by extraocular and orbicularis oculi muscle contractions. Muscle contractions and vitreous displacement that occur during an intraocular surgery, or with a penetrating eye wound, may cause expulsion of intraocular contents. Closure of the palpebrae may increase IOP anywhere from 10 to 50 mm Hg, depending on whether the closure is normal or forceful.[6]

Pupil Size

In mammals, iris musculature that controls pupil size is smooth muscle and is controlled primarily by the autonomic nervous system.[23] Parasympathetic stimulation of the iris constrictor muscle results in miosis (pupil constriction), and sympathetic stimulation of the iris dilator muscle results in mydriasis (pupillary dilation). In contrast, avian species have striated pupillary muscles, which are unresponsive to topically applied parasympatholytic or sympathomimetic agents.[24]

Pupils are inaccessible for anesthesia monitoring during ophthalmic surgery. Although the ophthalmologist may be able to provide information about pupil size during the procedure, pupil size as an indicator of anesthetic depth is not reliable.[25,26] Pupil size is of greatest concern in cataract-removal surgery, which requires the pupil to be widely dilated and the eye immobilized. Most anesthetic or sedative agents, with the exception of ketamine, will cause miosis.[1] Opioids have variable effects on pupil size among species[27,28] and may adversely affect the mydriasis required for cataract surgery.[29] An intramuscular combination of hydromorphone-acepromazine caused significant miosis in dogs at 10 and 25 min after injection.[30] Administration of opioid antagonists (i.e., naloxone) may reverse miosis when it occurs.[31] Prostaglandins, histamines, and other mediators of inflammation may cause miosis by a direct effect on the iris constrictor muscle.[26,32] Consequently, antiprostaglandins and antihistamines may be administered prior to intraocular surgery. Sympathomimetic, cholinergic, and anticholinergic drugs applied topically to the eye will affect pupil size. It has been suggested that mydriasis is more difficult to achieve after the onset of sedation or anesthesia,[29] whereas mydriasis achieved prior to anesthetic induction or sedation is usually unaffected by the miotic properties of anesthetic and sedative drugs.[1]

Globe Position

Globe motion during general anesthesia is not unusual, and position of the globe may vary among species and stages of anesthesia. However, motion is undesirable during corneal and intraocular surgery. Excessive manual traction to maintain a stable globe position may cause expulsion of intraocular contents or initiation of the OCR. In addition, eye reflexes that may be maintained during anesthesia in some species may also interfere with procedures. Paralysis with NMBs or retrobulbar regional anesthesia during general anesthesia should eliminate ocular reflexes and enable positioning of the globe without excessive manual traction, reducing the potential for expulsion of globe contents or initiation of the OCR.

Cardiovascular Physiology

Ocular patients are often elderly, with all the attendant problems associated with aging, such as loss of physiological reserve, preexisting disease, and chronic medication administration. The depth of anesthesia required for adequate depression of ocular reflexes and globe motion to facilitate intraocular surgery often results in pronounced hypotension and may represent additional risk for elderly patients.[3] Prolonged hypotension may predispose large animal patients to postanesthetic myopathy.[33] Balanced anesthesia combined with adjunctive anesthetic techniques, such as regional anesthesia or neuromuscular blockade, may allow a decrease in depth of inhalation anesthesia and a closer approximation of normal cardiovascular function.[3]

Oculocardiac Reflex

The OCR is a trigeminovagal (cranial nerves V and X) reflex that may be induced by pressure or traction on the eyeball, ocular trauma or pain, or orbital hematoma. Initiation of the reflex manifests as cardiac arrhythmias, which may include bradycardia, nodal rhythms, ectopic beats, ventricular fibrillation, or asystole.[16] The afferent pathway of the reflex follows ciliary nerves to the ciliary ganglion and then along the ophthalmic division of the trigeminal nerve. The afferent pathway terminates in the main trigeminal sensory nucleus in the floor of the fourth ventricle. The efferent pathway starts in the fibers of the vagal

cardiac depressor nerve, resulting in negative inotropic and conduction effects. Although OCR may occur most commonly during ocular surgery, it may also occur during nonocular surgery when pressure is placed on the eyeball.[16] It has been suggested that the more acute the onset, and the more sustained the pressure or traction, the more likely OCR is to occur. In people, OCR occurs most frequently during strabismus surgery in children and may be related to the degree of traction necessary to expose the medial rectus muscle during surgery.[16] Hypercapnia significantly increases the incidence of bradycardia in these patients.

Atropine administration to prevent or treat the OCR is controversial in humans.[16] Cardiac dysrhythmias may occur after atropine administration, especially in the presence of halothane, and may persist longer than the OCR response. In children, intravenous (IV) atropine or glycopyrrolate were more effective in preventing OCR than was intramuscular premedication with atropine, with glycopyrrolate producing less of a tachycardic effect than atropine.[34]

Bradycardia is the most common manifestation of OCR, although other dysrhythmias are possible, as already mentioned. Treatment of OCR should begin with discontinuing stimulation. The OCR ceases when stimulation ceases, so communication with the surgeon to discontinue procedural stimulation is vital if an OCR is suspected. Fortunately, it is possible for the OCR to fatigue with repeated, prolonged stimulation.[16] If bradycardia persists, treatment with atropine (0.02 mg/kg IV), or injection of lidocaine into the eye muscles to prevent transmission along the afferent limb of the reflex, may be effective.[3] Precautions against initiation of the OCR should include assuring an adequate depth of anesthesia, maintaining normocarbia, and gentleness of surgical manipulation.[16]

Ophthalmic Medications

Eyedrops are concentrated medications that may cause systemic side effects, especially when administered to very small patients. Systemic effects may be minimized by diluting topical medications and limiting their frequency of application.[4,16]

Cholinergic Agents

Glaucoma may be treated with cholinergic agents that decrease IOP primarily by increasing aqueous outflow. Direct-acting cholinergic agents are similar in structure to acetylcholine and produce effects similar to acetylcholine when absorbed systemically. Indirect-acting cholinergic agents are anticholinesterases. These facilitate the buildup of acetylcholine by slowing its enzymatic hydrolysis. Pilocarpine is a topical, direct-acting cholinergic agent commonly used in the treatment of glaucoma and may produce bradycardia or atrioventricular block if absorbed systemically.[1] These dysrhythmias may be similar to, and difficult to distinguish from, those produced by the OCR.[35] As mentioned in the section on neuromuscular blocking agents, to prevent prolongation of depolarizing neuromuscular blockade, anticholinesterase administration should be discontinued 2 to 4 weeks prior to succinylcholine administration.[35]

Adrenergic Agents

Adrenergic agonists and antagonists are both used to treat glaucoma. Although the exact mechanisms for decreasing IOP are not clear, it is believed that the agonists primarily increase aqueous-humor outflow, whereas the antagonists primarily decrease aqueous humor production.[1] Adrenergic agonists, such as epinephrine or dipivefrin, may predispose patients to catecholamine-induced cardiac dysrhythmias. Topical application of adrenergic agonists has been associated with increased HR and BP in people.[36]

Phenylephrine is an adrenergic agonist that is used to produce mydriasis prior to cataract surgery or in patients with uveitis. Subconjunctival phenylephrine has been associated with hypertension and pulmonary edema in a horse during anesthetic recovery.[33] In dogs undergoing cataract surgery, topical treatment with phenylephrine has been associated with arterial hypertension.[37] Topical application of 10% phenylephrine increased arterial BP and reflex bradycardia in normal dogs.[38] It has been suggested that the susceptibility of patients to the adverse effects of topically applied phenylephrine during anesthesia depends on several factors, including individual variability, frequency of application, concentration of the solution, and the anesthetic regimen.[39] Acepromazine may be useful in counteracting the hypertension produced by phenylephrine.[37,39]

Timolol, a nonselective ß-adrenergic antagonist that is commonly used to treat glaucoma, has been associated with more adverse systemic effects in people than have any other topically applied glaucoma medications.[40] Systemic effects in people may include bradycardia, hypotension, congestive heart failure, and exacerbation of asthma and myasthenia gravis.[16] Profound bradycardia has been observed in dogs after topical administration. Significant decreases in HR and BP have been observed in anesthetized dogs within 30 min of topical timolol administration.[41] Decreased IOP in both the ipsilateral and the contralateral eyes further substantiated systemic absorption of the drug. Timolol administration is contraindicated in animals with heart block, cardiac failure, or obstructive pulmonary disease.[41]

Carbonic Anhydrase Inhibitors

These inhibitors, such as methazolamide, decrease IOP by decreasing aqueous-humor production.[42] Carbonic anhydrase is found in other tissues besides the eyes, most notably the red blood cells and kidneys.[42,43] Administration of systemic carbonic anhydrase inhibitors impacts ion exchange in the kidneys, resulting in the retention of chloride and the excretion of bicarbonate and potassium. Treated patients may have metabolic acidosis and electrolyte imbalances, most notably hypokalemia and hyperchloremia. Some carbonic anhydrase inhibitors cause profound potassium excretion, as evidenced by the presence of hypokalemia despite metabolic acidosis that would typically be accompanied by hyperkalemia.[43]

Acidosis and electrolyte imbalances may disrupt cardiovascular and neurological function. Hyperventilation would typically occur during metabolic acidosis as a compensatory mechanism, but hypoventilation during anesthesia may exacerbate the metabolic acidosis by inducing respiratory acidosis.[44] Acidosis may increase the potential for cardiac dysrhythmias during anesthesia.

Ideally, metabolic acidosis and electrolyte imbalance would be corrected prior to anesthesia, and ventilatory support would be provided to prevent significant respiratory acidosis.

Osmotic Agents

Examples of osmotic agents for treatment of glaucoma include mannitol and glycerin. These agents are usually used to produce a rapid decrease in IOP in patients with acute or subacute glaucoma, and are usually administered immediately prior to surgery. Increased central venous pressure, increased serum osmolality, and pulmonary edema have been reported in dogs treated with mannitol.[45,46] The increase in osmolality may last for several hours. Although clinical pulmonary edema was not evident, histological evidence of pulmonary edema has been reported for dogs that received mannitol during methoxyflurane anesthesia.[47] It was suggested that pulmonary edema was less likely in patients being mechanically ventilated when compared with patients breathing spontaneously. Osmotic agents are not recommended in patients with preexisting cardiac or pulmonary disease, renal dysfunction, or dehydration.[1]

Corticosteroids

Prolonged topical eye or systemic administration of corticosteroids may depress adrenocortical function.[48,49] The need for corticosteroid supplementation in these patients prior to the stress of surgery and anesthesia has not been clearly determined. If hypoadrenocorticism is present, corticosteroids may be administered prior to anesthesia and surgery.[50,51] It should be remembered that the coadministration of corticosteroids and NSAIDs may exacerbate the toxicity of both classes of drugs.

Anesthetic Drugs

Inhalation Agents

Inhaled anesthetics reduce IOP proportional to the depth of anesthesia in human patients during controlled ventilation and normocapnia. Reductions of 14% to 50% have been noted.[16] Methoxyflurane has historically been the inhalation anesthetic preferred by ophthalmologists. It was believed to provide greater extraocular muscle relaxation, as well as a hypotonic and centrally rotated eye.[50,52] Additionally, the slower recovery from anesthesia was preferred for ocular patients. Methoxyflurane is no longer commonly used in veterinary patients. It has been replaced with halothane, isoflurane, and sevoflurane, which provide rapid induction and recovery. Rapid recovery, however, potentially increases the risk of iatrogenic trauma or intraocular bleeding. Appropriate preoperative or postoperative medication should be used to provide a slower, calmer recovery.

In human adults, halothane decreases IOP, but in a manner that is not dose dependent and has a ceiling effect.[53] Isoflurane effects on IOP are similar to those of halothane.[53] Halothane sensitizes the heart to catecholamines,[54] which may become problematic in ocular patients that receive topical adrenergic drugs. It is not unusual for ophthalmic surgeons to administer intraocular epinephrine to dilate the pupil and control intraocular bleeding during surgery. Epinephrine may be readily absorbed through ocular vasculature and produce systemic effects, such as cardiac tachydysrhythmias or premature ventricular beats, which may be exacerbated by halothane. In dogs and cats, the dysrhythmogenic dose of epinephrine is much higher when used with isoflurane,[54] possibly making it the preferred inhalation agent when used with exogenously administered catecholamines. It has been suggested that extraocular muscle relaxation and position of the globe are superior with isoflurane, but the information is anecdotal.[33]

Although there is little information on the ocular effects of sevoflurane in veterinary patients, it is presumed to have effects on the eye similar to those of halothane and isoflurane. In humans undergoing nonophthalmic surgery, IOP was decreased equally in those patients receiving sevoflurane when compared with those receiving propofol.[55] In patients undergoing elective ophthalmic surgery, IOP did not increase during sevoflurane and remifentanil anesthesia in response to tracheal intubation or laryngeal mask airway insertion.[56]

Nitrous oxide (N_2O) administration is contraindicated when intraocular gas or air injection is intended for a closed eye.[35,57] Air is sometimes injected into the anterior chamber of the eye to prevent synechia formation after corneal laceration or staphyloma repair. N_2O may diffuse into the intraocular air bubble, causing it to expand faster than the air can diffuse out, thereby increasing IOP. Sulfur hexafluoride (SF_6) may be injected into the vitreous space in retinal reattachment surgery and may expand to undesirable dimensions in conjunction with N_2O administration, resulting in increased IOP. It is recommended that if intraocular gas injection is intended in a closed eye, that N_2O be discontinued at least 15 to 20 min prior to injection. For repeat anesthetic episodes, it is also recommended that N_2O not be administered for at least 5 days after intraocular air injections and for 10 days after SF_6 injection.[35,57]

Injectable Anesthetic Agents and Adjuncts

Anticholinergic Agents

Administration of atropine or glycopyrrolate to canine ophthalmic patients is controversial.[50,58,59] One potential benefit is preventing the OCR, but anticholinergic administration may be undesirable in the presence of preexisting tachycardia. Conversely, anticholinergic administration may be appropriate in patients with preexisting bradycardia, or with concurrent administration of injectable drugs that may induce bradycardia (i.e., opioids and α_2-agonists). Cannulation of the parotid duct may be more difficult during parotid duct transposition surgery if anticholinergics are administered preoperatively.[60] The potential for colic in horses contraindicates the routine administration of anticholinergics.

Topically applied atropine produces cycloplegia, which decreases aqueous filtration, and mydriasis, which predisposes patients to filtration angle closure. Both of these effects will increase IOP in dogs and people with glaucoma, but the effects of systemically administered anticholinergics on pupil size and IOP are not clear. In people, systemically administered atropine or glycopyrrolate has no effect on IOP in normal patients, and atropine has no effect on IOP in people with glaucoma.[59,61] Atropine administered with neostigmine to reverse nondepolarizing neuromuscular blockade does not seem to increase IOP.[16]

Glycopyrrolate administered parenterally had no effect on pupil size or IOP in normal dogs, but the effects of atropine under similar circumstances was not investigated.[61] In a retrospective study of glaucomatous dogs, anticholinergic administration did not adversely affect IOP, but only 30% of the dogs in the study had received anticholinergic treatment.[61] It has been suggested that glycopyrrolate may have a lesser effect on pupil size and IOP than does atropine. This effect may be due to poor cellular penetration of end organs by quaternary ammonium compounds, such as glycopyrrolate, when compared with the tertiary amines, such as atropine. Consequently, the use of glycopyrrolate may be preferred in glaucoma patients requiring anticholinergic treatment.[59]

Barbiturates and Propofol

Thiopental and pentobarbital decrease IOP.[5,6] The mechanism for reduction is believed to be depression of the areas of the central nervous system (diencephalon) influencing IOP, and facilitation of aqueous outflow.[16] Thiopental decreases IOP in both normal and glaucomatous eyes.

Although chemically dissimilar, propofol has clinical properties similar to those of thiobarbiturates.[62] Studies in humans indicate that propofol decreases IOP and may negate the increase in IOP associated with intubation or the administration of depolarizing NMBs.[62] The effect of propofol on IOP in children is similar to that of thiopental during induction of general anesthesia.[63]

Etomidate

Although etomidate decreases IOP, etomidate-associated myoclonus may actually increase IOP.[3,16] It is recommended that etomidate not be used alone for induction, but rather in conjunction with a benzodiazepine muscle relaxant (i.e., diazepam or midazolam) in patients with penetrating eye wounds.

Dissociative Anesthetics

The effects of the dissociative anesthetics in ophthalmic patients are contradictory, both for human and veterinary patients. In people, early studies indicate that ketamine increases IOP, but ketamine does not affect IOP when administered after diazepam and meperidine. When administered intramuscularly, ketamine may even lower IOP in children.[5]

Ketamine induces extraocular muscle contractions, which may increase IOP in some species.[50,64] In horses, but not in dogs, prior administration of xylazine attenuates the increase in IOP.[64,65] In patients with the potential for globe rupture, such as a penetrating eye wound or deep corneal ulcer, the extraocular muscle contractions and increases in IOP are undesirable, suggesting that the use of ketamine should be avoided in patients when rupture of the globe is a concern.

Ketamine causes nystagmus, which may persist even when combined with xylazine, making ketamine unacceptable as the sole anesthetic for ophthalmic procedures.[50,65] The palpebrae remain open, the pupils dilate, and the palpebrae and corneal reflexes persist after ketamine administration.[25,66] Ocular reflexes also persist after administration of the anesthetic combination of tiletamine, a dissociative anesthetic, and the benzodiazepine zolazepam. Ketamine does not appear to decrease tear production in cats,[67] but the palpebrae remain open, which allows corneal drying and necessitates application of an ocular lubricant. Recoveries from ketamine administration can be very prolonged and uncoordinated, predisposing patients to ocular trauma.[50]

α_2-Adrenergic Agonists

Intramuscularly administered xylazine causes dogs and cats to vomit. Vomiting is less likely when xylazine is administered IV, but the potential still exists.[68] Consequently, xylazine should be used cautiously in patients with penetrating eye wounds.

Xylazine produces mydriasis in some species, possibly by inhibiting central parasympathetic tone to the iris or through stimulation of α_2-adrenoceptors located in the iris.[69] In cats, rabbits, and monkeys, it has been reported that xylazine decreases IOP by depressing sympathetic function and decreasing aqueous production.[70] In horses, two studies determined that IOP could be decreased by 23% with the administration of 0.3 mg/kg xylazine IV and by 27% with the administration of 1.0 mg/kg xylazine IV.[71,72]

Systemically administered xylazine may cause acute reversible lens opacity in rats and mice.[73] Topical application of xylazine produces cataract formation in the treated eye, whereas the contralateral eye remains unaffected. The mechanism for this effect is unknown. As mentioned previously, xylazine does not reduce tear production in dogs, but the combination of xylazine and butorphanol apparently works synergistically to decrease tear production significantly.[12] Xylazine does not decrease tear production in horses.[9]

Medetomidine is a more selective α_2-adrenergic agonist. Topical administration of medetomidine decreased IOP in cats and rabbits, while producing mydriasis, suggesting that there are α_2 receptors in the eye that are involved in the regulation of IOP.[74–76] In contrast, IV administration of medetomidine resulted in miosis in normal dogs, without a decrease in IOP.[77]

IOP was not affected by systemically administered medetomidine in dogs that had received tropicamide (an anticholinergic and cycloplegic agent) topically. The pupil size in these dogs increased after tropicamide administration and continued to increase slightly after medetomidine administration, although it was not determined whether the continued increase was exclusively caused by the medetomidine.[78] Lens opacification has not been reported after medetomidine administration. Medetomidine may be administered as a continuous-rate infusion (CRI) in ocular patients to provide profound sedation and moderate analgesia postoperatively. The effects of systemically administered α_2-agonists on IOP should be taken into consideration when tonometry is anticipated.

Benzodiazepines

Both midazolam and diazepam decrease IOP in dogs and cats after IV administration.[6,79,80] The IOP decrease may be related to the centrally acting muscle-relaxant properties of the benzodiazepines. One study suggests that diazepam may negate the increase in IOP that occurs after ketamine administration.[5]

Phenothiazines

Acepromazine is a sedative with antiemetic properties that may prevent vomiting and gagging in ophthalmic patients who have undergone intraocular surgery or have a ruptured eye. In horses, acepromazine has decreased IOP as much as 20%.[72] The longer action of acepromazine may be useful in providing a slower, quieter anesthetic recovery, thereby reducing the potential for postoperative trauma.

Analgesia

Ocular and periocular structures are richly innervated and highly sensitive. Symptoms of ocular pain include blepharospasm, photophobia, ocular discharge, rubbing of the eyes, and avoidance behavior. A variety of topical and systemic drug therapies are currently available to address pain management adequately in ophthalmic patients.

Opioids

Opioid selection for ocular patients should include consideration of quality of analgesia and appropriate duration of action. Opioids may be administered as a periodic injection or as a CRI.

Morphine decreases IOP, and other opioids are assumed to have the potential for a similar effect.[6] Emesis, and the associated increase in IOP, is a possible side effect of opioid administration. This may suggest that opioid administration should be delayed until the patient is anesthetized. Bradycardia, which may predispose patients to the OCR, occurs with some opioids and may necessitate administration of an anticholinergic. As mentioned previously, the effects of opioids on pupil size are variable among species.[27,28] Morphine produces miosis in dogs, rabbits, and people, and mydriasis in cats, rats, mice, and monkeys.[27,28]

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) can inhibit both isoforms of the cyclooxygenase enzyme: COX-1 and COX-2. Although there is significant overlap in COX isoform functions, COX-1 is important for normal physiological function of the gastrointestinal tract, renal system, platelets, and blood flow to specific tissues.[79] Cyclooxygenase 2 is produced in part by macrophages and inflammatory cells that have been stimulated by cytokines and other inflammatory mediators, and is considered to be associated with the production of inflammation and pain.[80] Most of the currently used NSAIDs in veterinary medicine inhibit both COX-1 and COX-2.[80,81] Other possible anti-inflammatory actions of NSAIDs include suppression of polymorphonuclear cell locomotion and chemotaxis through inhibition of leukotriene synthesis, decreased expression of inflammatory cytokines and mast cell degranulation, free-radical scavenging, and local anti-inflammatory effects caused by the accumulation of NSAIDs as organic acids at the site of inflammation.[79,82–84] The responsiveness of the feline cornea to chemical stimuli of polymodal nociceptors was diminished by NSAIDs, suggesting that corneal pain may be inhibited by NSAIDs.[85] This effect may be due not only to inhibition of cyclooxygenase activity, but also to a direct effect of NSAIDs on the excitability of polymodal nerve endings.

Both systemic and topical administration of NSAIDs are widely used in ocular patients, with flunixin being the most popular. NSAIDs effectively prevent intraoperative miosis, and control postoperative pain and inflammation after intraocular procedures, as well as controlling uveitis and alleviating pain from various other ocular conditions or disease processes.[86]

NSAIDs have been associated with decreased platelet aggregation, gastrointestinal ulceration and bleeding, and renal and hepatic damage.[87] Topical NSAID administration is associated with irritation of the conjunctiva, corneal cytopathy, decreased aqueous outflow, and its systemic absorption through nasal mucosa.[88,89] The use of NSAIDs in acutely inflamed canine eyes may increase IOP, possibly due to decreased aqueous outflow.[89] Corneal complications reported with topical use of NSAIDs in humans may be attributable to the solution's vehicle, solubilizer, or preservative, rather than the active drug itself.[79]

Coordination of systemic and topical NSAID application is essential to prevent excessive administration and toxicity. The NSAIDs should be used cautiously in geriatric patients, who often have preexisting renal and gastrointestinal disease.

Intravenous Lidocaine

In a preliminary study of dogs undergoing intraocular surgery, it was determined that lidocaine administered IV as a loading dose (1.0 mg/kg) followed by CRI (0.025 mg/kg/min) may provide preemptive analgesia similar to morphine administered IV as a loading dose (0.15 mg/kg) followed by CRI (0.1 mg/kg/h).[87] The exact mechanism for the analgesic effects of IV lidocaine in these patients has not been established, although inhibition of A-δ fiber and C-fiber discharges from sensory neurons of the eye may be involved.

Local and Regional Anesthesia

Local or regional anesthesia may be adequate for less invasive procedures or may be included as part of a balanced general anesthetic regimen. Topical anesthesia for diagnostic and therapeutic procedures in veterinary ocular patients usually requires accompanying sedation to gain cooperation of the patient. Topical anesthesia and sedation may be the preferred technique in ruminants and horses in which a standing procedure is anticipated or in other patients in which general anesthesia would be accompanied by unacceptable risk.

Local anesthetics applied topically are readily absorbed through mucous membranes.[1] Systemic toxicosis is possible, though unlikely, but administration to small patients should be judicious.[90,91] Topical anesthetics can be irritating and cause transient conjunctival hyperemia, as well as damage corneal epithelium, delay corneal wound healing, and mask signs of disease or discomfort.[1] It is recommended, therefore, that topical anesthetics be reserved for diagnostic rather than therapeutic purposes. Tear production and blink reflex will be reduced after topical anesthetic administration, necessitating the application of ocular lubricant to protect the cornea after completion of the procedure.[1]

Topical administration of 1% morphine sulfate solution ap-

pears to provide local analgesia in dogs with corneal ulcers.[92] The antinociceptive effect is possibly a result of interaction with μ opioid receptors, which have been identified in small numbers in normal canine corneas, and δ opioid receptors, which have been identified in the corneal epithelium and stroma of dogs. In contrast with the local anesthetics, this local analgesic effect is produced without delaying corneal wound healing or causing any discernible tissue damage.[92]

Administration of local anesthetic to the surface of an open wound is referred to as a *splash block*. Splash blocks may be used for intraoperative and postoperative analgesia in ocular patients (i.e., after enucleation). Bupivacaine (0.5%) is commonly used for this technique because of its longer action. The maximum dose should not exceed 2.0 mg/kg to avoid potential toxicosis. Epinephrine may be added to the bupivacaine (1:200,000) to reduce bleeding and delay systemic absorption. In a recent study assessing the duration of effect of topical local anesthetic administration, it was determined that two applications of 1 drop of 0.5% proparacaine, with a 1-min interval between drops, resulted in 25 min of reduced corneal sensation in dogs.[93]

Regional anesthetic techniques commonly used for ocular patients include auriculopalpebral nerve block, supraorbital nerve block, and retrobulbar injection. Techniques for these nerve blocks are described elsewhere in this text.[94]

The auriculopalpebral nerve, which is a terminal branch of the facial nerve (cranial nerve VII), provides motor innervation to the orbicularis oculi muscle. Blockade of the auriculopalpebral nerve eliminates forceful blepharospasms, thereby facilitating ocular examination or minor surgical or diagnostic procedures.[1] In horses, auriculopalpebral block has no adverse effects on tear production or IOP.[74,95]

The supraorbital nerve, which is a termination of the ophthalmic branch of the trigeminal nerve (cranial nerve V), provides sensory innervation to most of the superior palpebra. Blockade of this nerve is commonly performed in sedated horses for placement of a subpalpebral lavage tube, repair of a palpebral laceration, or other similar minor procedures.[1] Other sensory nerves that are less commonly blocked include the infratrochlear, zygomatic, and lacrimal nerves.

Retrobulbar or peribulbar injection can be performed as an adjunct to sedation or general anesthesia. Retrobulbar injection of local anesthetic will block the optic (cranial nerve II), oculomotor (III), trochlear (IV), ophthalmic and maxillary divisions of the trigeminal (V), and the abducens (VI) nerves. Blockade of these nerves causes desensitization of the globe and palpebrae, akinesia of the globe, transient vision loss, pupil dilation, and decreased IOP.[1] The Peterson eye block is a well-known example of a retrobulbar technique used in cattle for regional anesthesia. During general anesthesia, retrobulbar injection has also been performed in horses to eliminate ocular movement without the accompanying disadvantages of deeper planes of anesthesia.[33,96] Potential complications of retrobulbar injection include retrobulbar hemorrhage, trauma to the optic nerve or globe, intrathecal injection of local anesthetic, and death.[90] Retrobulbar injection has been advocated to prevent the OCR, but performance of the technique itself has the potential to elicit the OCR.[1,16] Large volumes of local anesthetic or orbital hemorrhage may cause either proptosis of the globe or displacement of the vitreous if the globe has been penetrated.[1]

Neuromuscular Blocking Agents

Paralysis of extraocular muscles relaxes the eye, allowing the globe to roll centrally and proptose slightly. These effects greatly facilitate positioning of the globe for ophthalmic surgery,[97,98] eliminating the need for significant surgical manipulation to obtain proper globe positioning and decreasing the potential for initiating the OCR.[58]

Depolarizing NMBs, such as succinylcholine, increase IOP just prior to paralysis in horses and people.[5,6,99] This effect may be due to an increase in choroidal vascular dilatation, or initial contraction of extraocular and orbital musculature. The increase in IOP subsides after approximately 8 min.[100] Although the increase in IOP would indicate that the use of succinylcholine should be avoided in patients with severely compromised eyes that are at risk for rupture, administration in patients with intact globes would seem reasonable as long as enough time was allowed for the increase in IOP to subside prior to incision.

Nondepolarizing NMBs do not appear to increase IOP.[35] Studies have indicated that vecuronium and pancuronium decrease IOP, whereas atracurium has no effect on IOP in people and dogs.[101–105]

As mentioned previously, indirect-acting cholinergic drugs are anticholinesterases that are used for treating glaucoma. Because anticholinesterases inhibit or inactivate the plasma pseudocholinesterases responsible for the metabolism of succinylcholine, they may cause prolonged paralysis.[106] It has been recommended that indirect-acting cholinergic drugs be discontinued 2 to 4 weeks prior to neuromuscular blockade with succinylcholine, although normal levels of plasma pseudocholinesterase activity may not be totally restored for 4 to 6 weeks.[35]

The effects of depolarizing NMBs are not reversible, whereas those of the nondepolarizing NMBs are reversible with anticholinesterases, such as neostigmine and edrophonium. Anticholinesterases are not associated with increases in IOP.[3] An anticholinergic (e.g., atropine or glycopyrrolate) is commonly administered prior to the anticholinesterase to prevent profound bradycardia in small animals and ruminants. Although the use of anticholinergics is usually avoided in horses, anticholinesterases may still be used for nondepolarizing NMB reversal, but should be administered very slowly while the HR is monitored. Alternatively, the use of nondepolarizing NMBs with a briefer action, such as atracurium, may be more desirable to avoid the need for reversal.[3] Neuromuscular paralysis reversal should be complete to prevent hypoventilation, struggling during recovery, self-trauma, and increases in IOP.

As mentioned previously, birds have striated rather than smooth iris musculature and may require paralysis to produce mydriasis. Topically applied parasympatholytic or sympathomimetic agents are ineffective in birds.[1] Intracameral injection of *d*-tubocurarine has produced mydriasis in pigeons.[107] Apnea and salivation occurred in raptors after intracameral injection of

muscle relaxants.[24] Topically applied vecuronium was found to produce the most consistent and greatest pupillary dilation in three species of psittacines with the fewest systemic side effects when compared with *d*-tubocurarine and pancuronium.[108] However, the differences in systemic side effects among the three psittacine species indicate that vecuronium should be used cautiously when applied bilaterally.

The use of sequential nondepolarizing and depolarizing NMBs is controversial.[3] In humans, a small amount of nondepolarizing NMB is administered first to block the initial muscle contractions of the depolarizing NMB. The depolarizing NMB is then administered to produce immobilization and allow intubation. Although this technique prevents coughing and gagging, and muscle fasciculations are not evident, IOP still increases during intubation.[16]

Increases in IOP may occur with increases in $PaCO_2$, necessitating mechanical ventilation, which may be facilitated by the administration of NMBs. It has been suggested, however, that hyperventilation may fail to decrease IOP because of the increases in intrathoracic and central venous pressure accompanying the use of mechanical ventilation.[105]

Electroretinography and Anesthesia

Electroretinography (ERG) is used primarily as a diagnostic test for progressive retinal atrophy or other degenerative retinal disorders, and to assess retinal integrity in dogs for which ophthalmoscopic evaluation of the fundus is not possible prior to cataract surgery.[109] Complete ocular akinesia is preferred during the ERG, which requires general anesthesia, and possibly neuromuscular blockade. The ERG requires dark adaptation of the patient and is performed in the dark, which makes anesthetic monitoring a challenge. There has been no standard generated for the ERG in unanesthetized patients.[109] Halothane and isoflurane depress the ERG in dogs, but the results are considered useful as long as the ERG for the patient and the control animal are generated under identical anesthesia conditions.[1,110,111] No single anesthetic protocol has been established for the performance of ERGs, although propofol induction with isoflurane maintenance has been used successfully in dogs.[112] Sedation and a cooperative patient may prove adequate for a semiquantitative ERG as is typically performed for preoperative screening of cataract patients.[1]

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