Key words: Intraocular pressure, ocular anesthesia, perforated globe.

Objectives:

1. Describe the various physiologic mechanisms that maintain intraocular pressure (IOP).

2. State the normal range for IOP and the effects various anesthetic agents have on it.

3. Describe the differences between the depolarizing and nondepolarizing muscle relaxants and their effects on IOP.

4. List the induction techniques that are effective for attenuating the increase in IOP associated with laryngoscopy and endotracheal intubation.

5. Develop an appropriate anesthetic plan for the patient undergoing surgery to repair a ruptured globe.

Anesthesia for the patient with a perforated globe can be complicated. Cognizance of the anatomy and physiology of the eye, including maintenance of intraocular pressure, is essential for the development of an anesthetic plan.

Since the induction phase of anesthesia is the most critical period during which intraocular pressure is affected, understanding the pharmacology of the various anesthetic agents and their effects on the eye is important. To avoid increasing intraocular pressure, a smooth, atraumatic induction is desired. However, methods to achieve this end may place the patient at risk for aspiration. Various techniques that attempt to accomplish this goal are described, including the use of narcotics, lidocaine, nitroglycerin, alpha (α₂) agonism, beta (β) adrenergic and calcium channel blockades, plus the laryngeal mask airway.

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Maintenance of intraocular pressure

Physiologic mechanisms maintain normal intraocular pressure (IOP) between 11 and 21 mm Hg. Pressure must be maintained within this range to ensure constant corneal curvature and a proper refracting index of the eye. Values higher than 25 mm Hg are considered pathologic and, in the case of a perforated globe, could lead to the expulsion of intraocular contents. Factors responsible for generating IOP can be grouped into 3 major categories: (1) aqueous humor fluid dynamics, (2) choroidal blood volume, and (3) extraocular muscle tone.

Aqueous humor

The primary physiologic mechanism that regulates IOP is the balance between the secretion and resorption of aqueous humor. This fluid, found in the anterior and posterior chambers of the eye, bathes and nourishes avascular structures of the eye. Aqueous humor is produced at a rate of 2 to 3 µL/min, and at any given time there is a total volume of 0.3 mL found within the posterior and anterior chambers.

Two thirds of the aqueous humor is an active secretory product of the carbonic anhydrase enzyme system within the ciliary body of the posterior chamber. The ciliary body has a folded structure that forms a relatively large surface area found just beneath a highly vascular area. Sodium ions are secreted actively into the spaces between the processes. Chloride ions follow. This creates an osmotic gradient pulling water from the surrounding capillaries, resulting in the formation of aqueous humor. The remaining one third is the result of simple filtration that occurs in the anterior chamber (Figure 1).

Once it circulates throughout the eye, aqueous humor exits by flowing into the spaces of Fontana, which lie between the cornea and the iris. It is then filtered though the trabecular meshwork to the Schlemm’s canal, ultimately draining into the right atrium (Figures 1 and 2).

The outflow of aqueous humor from the Schlemm’s canal follows the Hagen-Poiseuille’s law of fluid flow rate (Figure 3). Anything narrowing these spaces, such as glaucoma, debris that accumulates after intraocular hemorrhage, or infection, markedly increases the resistance to outflow, leading to an increase in IOP.

A major factor affecting the spaces of Fontana is pupil size. Dilated pupils narrow the spaces, increase resistance to aqueous outflow, and subsequently increase IOP. Constricted pupils have the
opposite affect by opening the angle, enhancing aqueous outflow, and thereby lowering IOP.

Ciliary muscle tone controls pupil size. If the ciliary muscle is relaxed, pupillary dilation occurs and impedes the flow of aqueous humor through the spaces of Fontana. Contraction of the ciliary muscle produces pupillary constriction, which opens the spaces and facilitates outflow.

The autonomic nervous system governs ciliary muscle tone. While sympathetic stimulation leads to relaxation of the muscle and subsequent pupillary dilation, parasympathetic innervation causes pupillary constriction. Although sympathetic stimulation leads to pupillary dilation, which theoretically leads to an increase in IOP, a concomitant vasoconstriction of the choroidal vessels occurs, resulting in a decrease in IOP.

**Choroidal volume**

The choroid plexus is a highly vascular layer of the eye comprised of numerous arterial anastomoses between the anterior and posterior chambers.\(^1\) This system autoregulates blood flow within perfusion pressures of 90 to 130 mm Hg to maintain a constant blood flow inside the eye.\(^1\) The principal mechanism for autoregulation is a change in the outflow of aqueous humor.\(^1\) It takes a few minutes to adjust to variations in blood flow, so that a sudden increase in arterial pressure will lead to a transient elevation in IOP.

The choroidal vessels drain into the venous plexus, then into the cavernous sinus. Therefore, central venous pressures (CVP) also affect choroidal blood volume. An increase in CVP will decrease the gradient for flow, thereby increasing choroidal blood volume and IOP. An example of this phenomenon is the rise in CVP and IOP associated with a cough or a Valsalva maneuver.

**Adrenergic responses in the eye.** The predominant adrenergic receptor found within the eye is the $\alpha$ receptor.\(^5,8\) The $\alpha_1$ receptor is the most abundant, with only a small $\alpha_2$ contribution.\(^9,10\) Few, if any, $\beta$ receptors have been located.\(^5,8,9,10\) The $\alpha$ receptor seems to exert control over choroidal blood flow with consequent influence over IOP by causing vasoconstriction of choroidal vessels.\(^5,6\)

Similar to other vessels, choroidal vessels are responsive to various chemical and thermal changes within the body.\(^4,13,15\) These responses are summarized in Table 1.

**Table 1. Intraocular pressure (IOP) changes associated with chemical and body temperature variations**

<table>
<thead>
<tr>
<th>Increase in IOP</th>
<th>Decrease in IOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory acidosis(^5,12)</td>
<td>Respiratory alkalosis(^5,12)</td>
</tr>
<tr>
<td>Hypoxia(^16)</td>
<td>Metabolic acidosis (associated with diabetes,(^13) exercise,(^14) and the administration of acetazolamide(^15))</td>
</tr>
<tr>
<td>Hyperthermia(^5)</td>
<td>Hyperbaric oxygen tensions(^16)</td>
</tr>
<tr>
<td>Hypothermia(^5) (although decreases viscosity, also causes vasoconstriction, which leads to a net reduction in IOP)</td>
<td></td>
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**Extraocular muscle tone**

Contraction of the extraocular muscles pulls the orbit toward the skull, causing the globe to be compressed against the socket. This leads to an increase in IOP, purely as a function of a mechanical process.

**Ocular muscles**

In 1966, Pilar and Hess\(^16\) reported the discovery that ocular muscles consisted of 2 predominant types of fibers, each with functionally different characteristics. The contractions produced by the combination of these 2 muscle types allows for fast, smooth, and complex movements of the eye.\(^17\)

The first and most dominant fiber found in an ocular muscle is the Fibrillenstrukturfiber. It is striated and singularly innervated.\(^5\) This large muscle fiber (20-50 µm in diameter) is similar to most mammalian skeletal muscles because each fiber reacts to an action potential in a typically “all-or-none” contractile response and is primarily responsible for saccadic (rapid, intermittent) movements of the eye.\(^6\) As the action potential is propagated down, the nerve fiber (which has a resting membrane potential of ~80 mV), it reaches well-defined neuromuscular junctions, called en plaque motor endplates, deep within the muscle fiber. Once the impulse reaches these terminals, a rapid contraction of the muscle occurs. The rate of contraction is so quick that these muscles are considered to be the fastest contracting of all mammalian muscles.\(^6\)

The second type of muscle fiber, the Felderstruktur fiber, is similar to the muscle fibers found in reptilian skeletal muscles.\(^6\) It is of concern to us because it is the one that responds differently to depolarizing muscle relaxants. This
fiber, which is predominantly responsible for the tonic contraction that supports the fixation of gaze, is different from the Fibrillenstruktur fiber in many ways. It is smaller in diameter (9-15 µm vs 25-50 µm) and has less sarcoplasm, fewer mitochondria, and a resting membrane potential of −40 mV. It has multiple nerve endings called “en grappe” neuromuscular terminals (which lie superficially within the muscle) and does not have a refined postjunctional apparatus. These multiple innervations lead to a response different from the all-or-none phenomenon characteristic of the Fibrillenstruktur fiber. It reacts to an impulse in varying degrees depending on the strength of the stimulus. The combination of these differences in contrast with the Fibrillenstruktur fiber ultimately lead to the production of a slow graded contraction in response to an impulse.

Kern, in 1965, reported the dissection Fibrillenstruktur and Felderstruktur fibers from superior rectus muscles of rabbits and treated them with acetylcholine. He reported that the Felderstruktur fiber responded with a contraction that was not only stronger, but also lasted considerably longer than that of the Fibrillenstruktur fiber (Figure 4). A contraction produced by this fiber can last up to 18 milliseconds, in comparison with the 5- to 8-millisecond contraction produced by the Fibrillenstruktur fiber.

Anesthesia and IOP

Succinylcholine and IOP. The slow, tonic contraction of the Felderstruktur fiber is of concern in anesthesia because of the way it responds to succinylcholine. Succinylcholine is a depolarizing muscle relaxant that has a chemical similarity to acetylcholine. It is able to bind competitively to nicotinic acetylcholine receptors at the postsynaptic membrane of the motor neuron. The result is a nonsynchronized depolarization of the cell membrane.

Unlike acetylcholine, however, succinylcholine is not metabolized by the surrounding acetylcholinesterase, enabling it to persist at the receptor for a longer period. By remaining at the receptor, the sodium channels of the postjunctional membrane remain open. The cell membrane of the muscle fiber is unable to repolarize, and the muscle eventually relaxes once calcium stores are depleted. This sequential action of succinylcholine produces the characteristic fasciculations seen after it is administered. Flaccid paralysis follows the fasciculatory period.

The quick onset and short duration of succinylcholine make it extremely advantageous in situations in which the airway must be secured rapidly. If the patient has a full stomach and requires emergency surgery, succinylcholine is an ideal relaxant to be used during the induction phase. Nevertheless, there are drawbacks. The major one that affects ocular surgery is the increase in IOP associated with the use of succinylcholine.

There is considerable evidence that the Felderstruktur muscle fiber’s response to succinylcholine is the cause of the increase in IOP. The acetylcholine-like effects of succinylcholine on multiple neuromuscular junctions lead to a sustained tonic contraction of the ocular muscles, which lasts longer than that of other skeletal muscles. The result of this tonic contraction is an increase in extraocular tension with consequent compression of the globe and a subsequent increase in IOP. An increase of up to 15 mm Hg above baseline has been demonstrated in unanesthetized volunteers after succinylcholine administration. The increase is apparent within 1 minute and peaks within 2 to 4 minutes. Another researcher demonstrated that IOP remained elevated for up to 6 minutes in healthy unintubated patients. Should a patient have a ruptured globe, this increase in IOP could force intraocular contents out of the eye. For this reason, controversy has arisen over the use of succinylcholine for a patient with the possibility of a perforating eye injury.

One study refuted the popular belief that the increase in extraocular muscle tension associated with succinylcholine has substantial contribution to the IOP elevation. Kelly et al measured IOP in 15 patients undergoing nonemergency enucle-
ation and compared IOP changes after the administration of succinylcholine in the diseased eye with the changes in the intact muscles of the unaffected eye, once all extraocular muscles of the damaged eye were detached. Detach ment of extraocular muscles theoretically prevents an increase in IOP by preventing the enhancement of extraocular muscle tone and subsequent compression on the globe.

Baseline IOPs were measured in the healthy and diseased eyes before and after the administration of thiopental sodium, 3 to 4 mg/kg. Once the loss of the eyelid reflex was noted, intubating conditions were achieved with 60% nitrous oxide, 40% oxygen, and halothane or isoflurane. No muscle relaxant was used. Mechanical ventilation was established to maintain end-tidal carbon dioxide concentrations of 35 to 38 mm Hg.

After the subjects were adequately anesthetized, the extraocular muscles of the diseased eye were severed, and 1.5 mg/kg of succinylcholine was administered. Intraocular pressure measurements were then taken in both eyes. Even with the extraocular muscles detached, IOP still increased substantially above baseline pressures in the diseased eye (Table 2).

The investigators concluded that extraocular contraction did not contribute to the increase in IOP associated with succinylcholine. The findings were explained as the result of succinylcholine’s cycloplegic action on the ciliary muscle, which caused an increase in outflow resistance of aqueous humor and subsequent elevation of IOP.

Other researchers, in an earlier study, proposed that the succinylcholine-induced increase in IOP was the result of choroidal dilatation. This theory was refuted by a study in which intraocular blood flow was measured before and after the administration of succinylcholine, and although there was a substantial increase in IOP, there was not an associated elevation in ocular blood flow.

The need for rapid induction of anesthesia is often a requirement for someone needing surgery to repair a ruptured globe. Such patients may be brought to the operating room with a “full” stomach, necessitating a rapid-sequence induction, yet the use of succinylcholine could also lead to extrusion of ocular contents and loss of vision. These conflicting issues have led to the development of anesthetic techniques that modulate the effects of succinylcholine in an attempt to provide safe rapid induction of anesthesia for patients with a perforating eye injury.

The most common method used to prevent the untoward effects produced by succinylcholine (eg, fasciculations, bradycardias, hyperkalemia, and myalgia) is pretreatment with a small dose of a nondepolarizing muscle relaxant. This technique has been tested during ocular surgery to determine its effectiveness in inhibiting the increase in IOP associated with the administration of succinylcholine. The results are inconsistent. Pretreatment with a nondepolarizing muscle relaxant cannot be relied on to consistently attenuate the increase in IOP.

Many studies indicate that pretreatment with a nondepolarizing muscle relaxant does not effectively attenuate the increase in IOP caused by the administration of succinylcholine, making this technique unreliable. Theoretically, if the elevation in IOP associated with succinylcholine is not related to the extraocular tension as Kelly et al demonstrated, it would explain why a dose of a nondepolarizing agent would be ineffective for preventing an increase in IOP.

Another method that has proved unpredictable for attenuating the IOP changes associated with succinylcholine is the use of a small, self-taming dose of succinylcholine before the administration of a full intubating dose. Not only is this method inconsistent in abating the response, but even the small dose of succinylcholine can produce a substantial rise in IOP.

Nondepolarizing muscle relaxants and IOP

Nondepolarizing muscle relaxants produce paralysis via competition for the nicotinic receptor at the postsynaptic neuromuscular junction. By blocking this receptor, ion flux is prevented from opening, thereby inhibiting depolarization. Flaccid paralysis is the result. Relaxation of the extraocular muscles secondary to the administration of a nondepolarizing muscle relaxant leads to a decrease in IOP unless consequential hypoventi-

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### Table 2. Measurement of intraocular pressure (IOP) after the administration of succinylcholine in intact and severed extraocular muscles

<table>
<thead>
<tr>
<th>Extraocular muscles</th>
<th>Baseline IOP (mm Hg)</th>
<th>IOP 90 s after succinylcholine (mm Hg)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact</td>
<td>15.1 + 1.0</td>
<td>25.2 + 1.6</td>
<td>.001</td>
</tr>
<tr>
<td>Severed</td>
<td>16.1 + 1.0</td>
<td>24.7 + 1.8</td>
<td>.001</td>
</tr>
</tbody>
</table>

Reprinted with permission by Kelly et al.24
lation results in choroidal vasodilation.\textsuperscript{11,31}

Rapid-sequence induction for penetrating eye injuries can be accomplished by the use of a nondepolarizing muscle relaxant. The newest of the nondepolarizing agents, rocuronium, is useful because intubating conditions can be achieved in 60 to 90 seconds. However, the resultant duration of action of all nondepolarizers is substantially longer than that of succinylcholine, potentially creating more harm than benefit for the patient with a difficult airway.

General anesthesia and IOP

Nonopioid and inhalation agents, with the possible exceptions of ketamine and etomidate, produce dose-related decreases in IOP. This decrease occurs for the following reasons: these agents (1) work directly on the central diencephalic control centers to decrease IOP, (2) facilitate drainage and inhibit production of aqueous humor, (3) relax extraocular muscles, and (4) work indirectly by affecting the cardiovascular and respiratory systems.\textsuperscript{3}

Propofol seems to be marginally better than thiopental in its ability to lower IOP following induction of anesthesia and attenuate a subsequent increase of IOP following the use of depolarizing muscle relaxants and the stress of laryngoscopy.\textsuperscript{22,34} The effect is multifactorial: propofol reduces systemic resistance and systolic arterial pressure to a greater extent than does thiopental.\textsuperscript{22,34}

Ketamine has been thought to increase IOP secondary to the sympathomimetic increase it produces in arterial pressure and CVP. Research, however, has demonstrated that ketamine, 2 mg/kg, in conjunction with the use of diazepam, 0.9 mg/kg, and meperidine, 0.9 mg/kg (as premedications), has no effect on IOP or is associated with a decrease in IOP.\textsuperscript{25}

When given in combination with atracurium, 0.6 mg/kg for induction of anesthesia, ketamine at a dose of 2 mg/kg has not been shown to increase IOP.\textsuperscript{26} One possible explanation for the lack of increase in IOP is the histamine release that follows atracurium administration, which could lead to vasodilation, thereby counteracting the increase in blood pressure associated with ketamine.

There have also been conflicting results with the use of etomidate and its effect on IOP. Etomidate can produce myoclonic activity, which may increase extraocular muscle tone and lead to an increase in IOP.\textsuperscript{37} In contrast, other investigators have demonstrated a decrease in IOP when etomidate was used in doses of 0.3 mg/kg with atracurium, 0.6 mg/kg, for the induction of anesthesia.\textsuperscript{56}

The effect of ventilatory methods on IOP during general anesthesia has also been studied.\textsuperscript{37} There were no differences in IOP noted in patients who were mechanically ventilated with positive pressure and those who remained spontaneously breathing.\textsuperscript{37} One must remember, though, the importance of maintaining a deep state of anesthesia to prevent incidental coughing or bucking in response to the endotracheal tube.

Endotracheal intubation and IOP

While much of the literature focuses on the effect of succinylcholine on IOP, it seems that the increase in IOP associated with the response to endotracheal intubation may be more substantial. Studies have revealed a direct relationship with an increase in the mean arterial pressure that accompanies intubation and an increase in IOP.\textsuperscript{30,38,39}

Several investigators have compared measurements of IOP and hemodynamics at different points of induction during the use of thiopental and succinylcholine or a nondepolarizing muscle relaxant.\textsuperscript{22,30,38,39} Thiopental decreased IOP below preinduction levels. When succinylcholine was given, IOP increased, but never above baseline measurements.\textsuperscript{22,30,38,39} The IOP response to intubation, however, was considerably greater. Mean arterial pressure and IOP increased substantially above baseline pressures, even in subjects who did not receive succinylcholine.\textsuperscript{22,30,38,39}

Endotracheal intubation increases IOP to a greater extent than does succinylcholine administration \textsuperscript{22,30,38,39} and exaggerates the rise in IOP associated with the use of succinylcholine.\textsuperscript{22} Although intubation causes a larger increase in IOP, when preceded by succinylcholine, it does not prolong the 6- to 8-minute duration of the elevation related to succinylcholine administration.\textsuperscript{22}

Coughing, bucking, or straining secondary to light anesthesia during laryngoscopy cause a transient, yet substantial elevation in CVP, with a consequent increase in IOP. These responses could be more detrimental to the intraocular contents than the use of succinylcholine as a muscle relaxant. Therefore, it is critical to ensure an adequate depth of anesthesia before attempting intubation.

As stated previously, nonopioid induction agents produce dose-related decreases in IOP. Higher doses of thiopental (ie, 5-6 mg/kg) or propofol (ie, 1.5-2 mg/kg) are more capable of providing the deeper state of anesthesia necessary
for intubation of a patient with a penetrating eye injury.\textsuperscript{22,30,32,34,38,39} When either is used as the sole induction agent in combination with succinylcholine, however, the increase in IOP associated with endotracheal intubation is not effectively blunted.\textsuperscript{30,34}

In one study, 60 ASA physical status I or II subjects undergoing elective ophthalmic surgery without preexisting increased IOP received an average dose of thiopental (4.9 mg/kg) or propofol (2 mg/kg) after being premedicated with diazepam (5-10 mg orally).\textsuperscript{34} Succinylcholine, 1.0 mg/kg, was the muscle relaxant used. Immediately before intubation, half of the subjects received an additional dose of thiopental (2.0 mg/kg) or propofol (1 mg/kg). The IOP decreased below baseline after induction and increased slightly after succinylcholine administration in all subjects (not above baseline, however). With the exception of subjects receiving a second dose of propofol, all had a significant ($P<.05$ to .001) increase in IOP above baseline (2-3 mm Hg) one minute after intubation.\textsuperscript{34}

When the study was repeated replacing succinylcholine with vecuronium, 0.1 mg/kg, IOP again decreased below baseline in all subjects after induction of anesthesia. There was, however, no increase after administration of the muscle relaxant, and IOP did not increase above baseline after intubation in any subject.\textsuperscript{32,33}

Techniques that attenuate the hemodynamic response (ie, tachycardia and elevated arterial pressure) associated with endotracheal intubation have been studied to determine their ability to prevent increases in IOP. These methods include the use of opioids, lidocaine, nitroglycerine, $\alpha_2$ agonists, calcium channel blockers, $\beta$-adrenergic blockers, and the use of a laryngeal mask airway (LMA).

**Techniques to attenuate the increase in IOP associated with intubation**

- **Opioids.** Opioids lower systemic vascular tone, which decreases arterial blood pressure and venous return. Their use during induction of anesthesia is an excellent method to attenuate an increase in IOP associated with intubation. All short-acting opioids have the ability to maintain mean arterial pressure and IOP below baseline measurements, even after intubation.\textsuperscript{30,36,38-42}

  Alfentanil at a dose of 15 $\mu$g/kg has been studied for its effect on IOP when given as a coinduction agent along with thiopental, 3 to 4 mg/kg. The methodology included the use of succinylcholine, 1.5 mg/kg, for endotracheal intubation. The study revealed a decrease in IOP after induction. The IOP increased after succinylcholine was given, although no higher than preinduction measurements, and it did not increase any higher once the trachea was intubated.\textsuperscript{39}

  One group of researchers concluded that a reasonable anesthetic technique for penetrating eye injuries might include thiopental (5 mg/kg) and alfentanil (20 $\mu$g/kg), followed by vecuronium 0.15 mg/kg.\textsuperscript{41} This combination effectively blocked the systemic blood pressure and heart rate changes associated with endotracheal intubation in 48 ASA physical status I to III patients undergoing cataract extraction and lens implantation.\textsuperscript{41} The investigators, however, failed to measure IOP, which raises questions about the external validity of their study.

  Researchers studying the effects of alfentanil and fentanyl on IOP have found no significant differences between the opioids in their ability to reduce the IOP response to endotracheal intubation.\textsuperscript{42} This opioid study compared IOP in 40 ASA physical status I or II patients undergoing routine ophthalmic surgery after premedication with diazepam, 5 to 10 mg, and induction with thiopental, 2 to 4 mg/kg, followed by succinylcholine, 1.5 mg/kg.\textsuperscript{42} The subjects randomly received fentanyl, 2.5 $\mu$g/kg, or alfentanil, 10 $\mu$g/kg, in addition to thiopental for induction of anesthesia. The vocal cords were sprayed with lidocaine, 1.5 mg/kg, after satisfactory neuromuscular relaxation was achieved.\textsuperscript{42} The IOP decreased significantly ($P<.05$) below baseline after induction of anesthesia in all subjects. It increased after succinylcholine administration but remained well below baseline. After intubation, the IOP rose to levels just below baseline and never increased higher than the initial measurements in any of the subjects.\textsuperscript{42}

- **Lidocaine.** Intravenous lidocaine given approximately 90 seconds to 7 minutes before laryngoscopy in doses of 1 to 2 mg/kg has the ability to block sympathetic responses to endotracheal intubation and has been studied extensively for its effectiveness in blunting an increase in IOP.\textsuperscript{22,43-47} Lidocaine administered in doses of 1.5 to 2 mg/kg in conjunction with thiopental, 3 to 5 mg/kg, and succinylcholine, 1 to 1.5 mg/kg, has been shown to prevent the increase in IOP noted after endotracheal intubation.\textsuperscript{43,44} In unpremedicated children, doses of lidocaine, 1.5 mg/kg, in combination with thiopental, 5 mg/kg, pancuronium, 0.15 mg/kg, and atropine, 0.02 mg/kg, adequately abated an increase in IOP after the induc-
tion of anesthesia and endotracheal intubation.44 Doses below this range gave inconsistent results.22,45

Another method of administering lidocaine is by a handheld nebulizer. In one study, 20 ASA physical status I or II patients were premedicated with diazepam and then given isotonic sodium chloride or 6 mg/kg of nebulized lidocaine.46 Induction of anesthesia was then achieved with enough thiopental to inhibit the eyelash reflex. Once this was accomplished, succinylcholine was given in a dose of 1.5 mg/kg. Compared with the control group, the investigators found lidocaine maintained IOP below preinduction levels after intubation.

Nitroglycerin. Nitroglycerin lowers systemic vascular resistance, especially venous tone. This leads to a decrease in arterial pressures and CVP, with a possible reflexive increase in heart rate. In one clinical investigation, hemodynamic variables and IOP were compared in 30 ASA physical status I or II patients who received 2 mg of nitroglycerin (0.5 mg tablets crushed and mixed with 3 mL of isotonic sodium chloride) or 3 mL of isotonic sodium chloride intranasally via an intravenous cannula 2 minutes before the induction of anesthesia.48 Hemodynamic parameters and IOP were measured before and after induction and after intubation. In all subjects, arterial blood pressure and IOP were lower after the induction of anesthesia. In the subjects who received nitroglycerin, arterial blood pressure decreased further than in subjects who received isotonic sodium chloride, and heart rate increased slightly. Blood pressure and IOP never exceeded preinduction measurements in the subjects who received intranasal nitroglycerin.49

In these same subjects, blood pressure and heart rate returned to baseline within 5 minutes. The IOP, however, remained lower than preinduction measurements for several more minutes.46 This would indicate a mechanism other than just the decrease in vascular tone as the explanation for the reduction in IOP associated with nitroglycerin. The authors suggested that the prolonged decrease in IOP may be the result of nitroglycerin’s ability to relax smooth muscle.48 They contend that nitroglycerin also may relax the orbicularis oculi muscle, thereby decreasing the muscle tone of the eye and subsequently lowering IOP.48

Alpha2 agonists. Stimulation of postsynaptic α2 receptors causes a depression of sympathetic activity via the cardiovascular control centers of the central nervous system.49 This leads to a decrease in adrenergic tone and vasodilation. In the eye, the reduction in vascular tone produces a subsequent reduction in choroidal blood volume and IOP.50,51

Clonidine is an antihypertensive drug that exerts its action primarily by stimulation of the postsynaptic α2 receptors. It also has some α1 agonistic properties. When given intravenously, it produces hypertension through α1 mediated vasoconstriction, but if given orally, the α2 effects predominate and vasodilation occurs.52 In the eye, α2 agonism also reduces aqueous humor production and enhances aqueous outflow by decreasing venous pressures.53 The result is a reduction of IOP.

When given orally 90 to 120 minutes before ophthalmic surgery, clonidine lowers anesthetic requirements and prevents IOP increases during laryngoscopy.54 This was apparent in one study in which patients received clonidine 5 µg/kg as a premedication before cataract surgery and then were induced with a combination of thiopental and vecuronium.55 The IOPs were below baseline 60 seconds after intubation and remained below preinduction levels for the duration of surgery.50

Clonidine may be a suitable premedication for the patient with a ruptured globe, although it is important to consider the time to its peak effect. It may not be possible to wait the 90 to 120 minutes necessary to obtain the maximum benefit from clonidine. It would also be interesting to repeat the study with the use of succinylcholine as the relaxant of choice to determine clonidine’s effectiveness in attenuating the increase in IOP associated with administration of succinylcholine.

A newer α agonist, dexmedetomidine, is similar to clonidine in its action on the central nervous system but is highly α2 selective, hence, it can be given intravenously without the concern of α1 mediated vasoconstriction.56 Researchers have demonstrated that dexmedetomidine, 0.6 µg/kg, administered at the induction of anesthesia abates the hemodynamic changes and increases in IOP in response to laryngoscopy.57 Specifically, IOP remained well below baseline, and plasma catecholamine levels were significantly reduced (P < .001) in subjects who received dexmedetomidine in comparison with the control group, who received only saline.54 Similar to a previous IOP clonidine study,58 a nondepolarizing muscle relaxant was used to produce adequate relaxation for laryngoscopy. More studies are needed to substantiate the use of dexmedetomidine during a rapid-sequence induction.
**Calcium channel blockers.** Smooth muscle contraction depends on the flow of calcium into the cell. Blockage of the calcium channels decreases the strength of contraction and leads to a decrease in vascular tone with a subsequent reduction in systemic vascular resistance and blood pressure.

Nifedipine is a calcium channel blocker that is effective for attenuating the hemodynamic response to laryngoscopy. The effect of sublingual nifedipine on IOP after induction of anesthesia and the administration of succinylcholine has been studied. Doses of 10 mg given sublingually 20 minutes before the induction of anesthesia with thiopental, 3 to 4 mg/kg, have adequately blunted the elevation of IOP after intubation with succinylcholine, 1.5 mg/kg. This technique can be applied clinically for the patient needing a rapid-sequence induction for emergency repair of a ruptured globe. If time permits, nifedipine can be a useful adjunct to the induction of anesthesia.

**Beta blockers.** Esmolol is a selective β-adrenergic antagonist. It primarily affects heart rate, with less effect on myocardial contractility or systemic vascular resistance. It blunts the hemodynamic responses to intubation and has been studied to establish its ability to block the increase in IOP.

The administration of esmolol, 1.5 mg/kg, before laryngoscopy did not attenuate an increase in IOP when given in conjunction with alfentanil, 10 µg/kg, thiopental, 5 mg/kg, and succinylcholine, 1 mg/kg, to 20 ASA physical status I or II women scheduled for laparoscopic surgery. This combination was effective for blunting an increase in heart rate, but mean arterial pressures and IOP increased significantly (P < 0.05) above baseline. The authors gave no explanation, but the β selectivity of esmolol at aforementioned doses is associated with unopposed α stimulation; combined with the lack of β receptors in the eye, may explain why it was not capable of preventing the increase in IOP associated with intubation.

**Laryngeal mask airway.** The use of the LMA has been advocated as an alternative to endotracheal intubation for prevention of the hemodynamic response and the increase in IOP associated with laryngoscopy during elective intraocular surgery. Some researchers have recommend the use of the LMA in place of endotracheal intubation for emergency eye surgery.

Studies have revealed that the insertion of the LMA is less stimulating than endotracheal intubation and prevents increases in IOP as measured by application pneumatonograph or an application tonometer. Each of these devices has been validated for accurate assessment of IOP. One such study compared IOPs in unpremedicated children in whom anesthesia was induced with halothane and atracurium, 0.5 mg/kg, and the airway was secured with LMA placement or endotracheal intubation. They reported a decrease in IOP after induction and less of an increase after insertion of the LMA in contrast with laryngoscopy and intubation.

In two other studies, IOP measurements taken after the insertion of the LMA were significantly lower (P<.01) than those taken after endotracheal intubation. The authors of these studies reported that IOP was lower in the subjects who had placement of an LMA compared with a laryngoscopy for endotracheal intubation. Other investigators, however, had notably different results, in which insertion of the LMA produced intraocular changes similar to those produced by laryngoscopy.

The varied methods of induction help clarify the difference in results. The investigators whose results revealed that the LMA was capable of preventing IOP increases included low-dose opioids in their induction. One group of investigators performed induction of anesthesia with enough thiopental to abolish the eyelid reflex, vecuronium, 0.1 mg/kg, and alfentanil, 7 µg/kg, while others induced anesthesia with etomidate, 0.2 mg/kg, vecuronium, 0.1 mg/kg, and alfentanil, 12 µg/kg. Both doses of alfentanil are lower than the dose needed to abate the IOP response to endotracheal intubation. However, the insertion of the LMA is less stimulating than laryngoscopy, so the use of alfentanil could have affected the results, raising questions about the internal validity of the study.

In one study, opioids were avoided all together; anesthesia was induced with enough propofol to inhibit the eyelid reflex in combination with vecuronium, 0.1 mg/kg. These investigators reported no differences in IOP after insertion of the LMA compared with intubation. These results support the argument that nonopioid induction agents alone are insufficient to prevent increases in IOP associated with the stimulation of laryngoscopy, and they do not seem to be sufficient for blunting the sympathetic IOP response to LMA insertion.

It seems that the LMA in combination with opioids or after induction of anesthesia with halothane (in pediatric patients) is a satisfactory alternative.
technique for the patient with a perforated globe injury. Whether inhalational induction with sevoflurane in the adult patient will afford similar protection for modulating IOP remains to be determined. It must be remembered, though, that the LMA is contraindicated for patients at risk for aspiration, which argues against the recommendations of some investigators who state that the LMA is suitable for emergency ocular surgery.  

Summary  
To provide safe anesthesia for a person who has a penetrating eye injury, it is important to avoid the increases in IOP associated with succinylcholine and endotracheal intubation. The most effective approaches to achieve this task are as follows: (1) achieving an adequate depth of anesthesia before instrumentation of the airway, (2) lowering the IOP before administering succinylcholine or attempting intubation, and (3) maintaining hypocapnia.

For the patient at risk for aspiration or whose airway is potentially difficult to manage (in which an awake intubation is contraindicated), a rapid induction of anesthesia can be performed best as follows: (1) achieving an adequate depth of anesthesia and decrease in IOP have been accomplished before administration of succinylcholine and before intubation is attempted. The judicious use of induction agents in addition to the use opioids, lidocaine, or both would seem sufficient for preventing damaging increases in IOP. Other effective choices could include intranasal nitroglycerine, calcium channel blockers, and $\alpha_2$ agonists.

If the airway is not a problem, the use of nondepolarizing muscle relaxants helps prevent increases in IOP. It is still important, however, to ensure a deep level of anesthesia before attempting endotracheal intubation. Opioids, lidocaine, and other medications can be used to blunt the IOP response to intubation.

If the patient is not at risk for aspiration, the LMA is a suitable alternative to intubation and may be effective for attenuating drastic increases in IOP. Nevertheless, insertion of the LMA still results in IOP increases that could be damaging to the eye, so it is important to block this response. The use of low-dose alfentanil is one approach that has been studied and found effective for this purpose.

Several effective techniques prevent detrimental increases in IOP. Although it is important to be aware of these methods, it is equally important to consider each situation individually and tailor the anesthesia plan accordingly.

REFERENCES  


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