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REVIEW ARTICLE

Contemporary Anesthesia Perspectives for Ophthalmic Surgery: A Brief Review

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ABSTRACT

In recent decades there have been few changes in the anesthesia management of eye surgery. By contrast, the 21st Century has witnessed major advancements in ophthalmic surgery with the adoption of minimally-invasive techniques, technologic innovations, and an expanding population seeking eye care. These factors have impacted intraoperative exposure such that many procedures are now performed on more complex patients, and completed in quicker time. Furthermore, in pursuit of economic savings and patient satisfaction there is a trend to divert eye surgeries away from the in-hospital setting to ambulatory centers or office locations. From an anesthesia perspective, these changes have imposed a demand on providers to shorten operating room turnover times and accelerate patient discharge while maintaining high standards of patient safety. This review will address five new avenues of anesthesia care, each of which offer possibilities in accommodating facets of this new order surgical experience. First, remimazolam is an ultra-short acting benzodiazepine that produces a predictable period of hypnosis and rapid, full recovery of consciousness because of its short context-sensitive half-time and inactive metabolites. A single 3-5 mg dose produces 11-15 minutes sleep that may be ideal for brief ocular interventions. Second, nasal CPAP/BiPAP and high flow nasal oxygen devices expand the profile of patients appropriately managed at an ambulatory center. Since their application improves arterial oxygenation and delays the onset of apneic hypoxemia, they are advantageous for patients afflicted by morbid obesity or severe obstructive sleep apnea. Third, open globe injuries have traditionally been managed under general anesthesia. However, recent studies attest to regional anesthesia as a viable alternative for many ocular insults, particularly for the elderly and patients with major organ dysfunction or risk for pulmonary aspiration. Fourth, the sub-Tenon block is a cannula-based regional ophthalmic skill performed predeominantly by ophthalmic surgeons because it necessitates conjunctival incision and dissection. Recently described variations of an incision-free, easily mastered sub-Tenon approach are likely to be included in residency and fellowship instruction, and so become an invaluable component of the anesthesiology armamentarium. This review concludes with a concise overview of the α_2 agonist dexmedetomidine with the focus directed on its uses as an adjunct for adult sedation, and advantage in children for premedication and control of emergence delirium.

Introduction

The corollary of advances in ophthalmic surgical technique and availability of more sophisticated equipment has been a shift in eye surgery venue away from the in-hospital setting to the office or ambulatory center. From an anesthesia perspective, the ramifications of this altered dynamic are patient and economic demands for improved safety, shorter operating room (OR) turnaround intervals, and early discharge. Consequently, many ophthalmic interventions are now managed under regional anesthesia with monitored anesthesia care (MAC). In response to these requirements, anesthesiologists must adapt and restructure their management plans looking to alternative regional techniques and short-acting medications that promote rapid awakening and accelerated street-readiness. This brief review addresses five topics which offer potential in meeting these goals.

Remimazolam

Advancements in ophthalmic surgical technique and equipment have resulted in reduced surgical times and increased demand on anesthesiologists for sedation profiles that facilitate improved turnaround without compromise of patient safety. Hypnotic medications are used in the perioperative period to allay anxiety, induce sleep, and assure a modicum of amnesia. The ideal properties of a sedative include rapid onset, swift recovery, and absence of residual effects. In recent decades, benzodiazepines have been widely used in procedural sedation, general anesthesia, and intensive care (ICU) management because they exhibit many of these attributes. In addition, their propensity to produce minimal cardiorespiratory depression has made them favorite adjuncts for procedural sedation in the ambulatory setting.

Remimazolam is a new generation benzodiazepine that contains a rapidly hydrolyzed and cleaved ester linkage. This produces an inactive metabolite which is rapidly eliminated in a manner akin to the ultra-short acting opioid, remifentanil.[1] Remimazolam can be administered either as a single bolus for brief interventions or continuous infusion providing the hypnotic component of a balanced anesthesia technique. The major benefit of remimazolam over say, midazolam, is that it affords a precise duration of hypnosis, a predictable elimination time and complete awakening because its breakdown metabolites lack sedative effects.[2] The ability to accurately control the hypnotic effects of remimazolam offers value to anesthesia providers, especially in clinical settings where rapid turnover times are prized. Expedient OR turnaround confers benefits such as cost savings, improved patient satisfaction and earlier discharge.[3]

The past decade has witnessed an increasing trend to shift eye surgeries away from in-hospital venues to ambulatory centers or ensuite office locations. Consequently, anesthesia providers face the challenge of minimizing the residual effects of sedation to expedite patient discharge. Furthermore, metabolite activity imposes restrictions on later patient activities such as driving and operating machinery. While remimazolam is approved in the USA for procedures of less than 30 minutes duration, there is no time constraint for administration in the European Union (EU).[4]

Remimazolam is rapidly metabolized after IV administration with a terminal half-life of 37-53 minutes.[5] The efficacy of remimazolam for induction and maintenance of procedural sedation has been evaluated in several randomized, double blind, multicenter studies for procedures such as colonoscopy and bronchoscopy.[6-7] All studies support the efficacy of remimazolam with a reported success rate (measured by predefined parameters) of >80%. Remimazolam produces deep hypnosis within 5 minutes of administration and its effects last between 11 and 15 minutes. The hypnosis interval may be potentiated by co-administration of low dose opiates, such as fentanyl (0.5mcg/kg).[8] Ready to discharge times are in the range of 50-64 minutes.[9] The context-sensitive half-time of remimazolam is insensitive to the duration of infusion, reaching a maximum value of 7-8 minutes after 2 hours.[10] The recommended induction dose of remimazolam is 5mg administered over 1 minute but should be customized on an individual basis. In general, doses of 2.5 mg or less may be sufficient for the elderly or those with hepatic impairment because of altered pharmacokinetic profiles. As with other sedatives, patients require constant monitoring of vital signs. Currently, propofol is the most widely administered intravenous agent for procedural sedation. By comparison, remimazolam is less likely to produce respiratory or hemodynamic depression. Additional advantages over propofol include (1) minimal pain on injection, (2) limited potential for pharmacokinetic drug interactions, (3) low accumulative effects with prolonged administration, (4) consistent clearance by tissue esterases across different patient populations, and (5) reversal with flumazenil. Disadvantages include cost, reconstitution of powder and wastage with single bolus administration.

To date, there are no studies evaluating remimazolam for sedation during eye surgery.

Remimazolam may be the ideal sedative for specific eye surgeries because it provides rapid-onset hypnosis and accelerated emergence. However, there is a learning curve associated with proficiency in its use. Considering these parameters, remimazolam is probably best suited to short duration eye procedures, such as uncomplicated cataract extraction or cyclophotocoagulation (CPC). Repeat IV boluses or infusions are appropriate for procedures extending beyond 15 minutes.

Open Globe Injury

Eye injuries are a principal cause of unilateral blindness. Worldwide, the annual incidence of ocular trauma is estimated to exceed 50 million cases. Of these, about 40% will result in decreased visual acuity and 3-5% in blindness.[11] Open globe injuries (OGI) are challenging emergencies for ophthalmologists and anesthesiologists, alike. They are classified according to the Birmingham Eye Trauma Terminology System (BETTS) which divides eye trauma into three anatomical zones (1,2 and 3).[12] Currently, there is considerable variation in the management of OGI, and the preferred mode of anesthesia is often governed by local or institutional guidelines.

However, recent surveys suggest that irrespective of zone, general anesthesia remains a preferred management option for OGI.[13] Anesthesiologists are singularly concerned about potential for extrusion of eye contents secondary to increased intra-ocular pressure (IOP) during injection of local anesthetic (LA).[14] However, concerns about patient comorbidity, airway anomalies or risk of aspiration may preclude immediate administration of general anesthesia. In addition, GA conveys inherent hazards because maneuvers such as straining, coughing, and retching significantly increase IOP, and jeopardize visual outcome. For example, a single dose of succinylcholine (a neuromuscular blocking agent administered for intubation) raises IOP in the intact eye by 1 to 8 mm Hg. Furthermore, coughing on the endotracheal tube may transiently increase IOP by as much as 35 mm Hg. Prudent patient selection coupled with slow administration of regional anesthesia under direct globe visualization may facilitate stricter control over IOP increases than general anesthesia and endotracheal intubation.

In 2002, Scott et al published a retrospective review of 220 open-globe injuries managed under either general or regional anesthesia.[15] In this study which specifically addressed intra and postoperative ocular complications, GA was administered in 36% cases and regional block in 64%. Patients with an intraocular foreign body, anterior wound or better visual acuity on presentation were more likely to receive an eye block and MAC. Of significance, no intra or post-operative complication was deemed attributable to mode of anesthesia. In a later study, Scott et al reviewed a further 238 OGI and compared visual outcomes in relation to regional versus general anesthesia.[16] This study found no difference in terms of improvements in post versus pre-operative visual acuity between the two groups. Moreover, McClellan et al performed a retrospective review of 448 OGI at their institution over an eleven-year period.[17] They concluded that, for any single zone of injury, neither regional nor general anesthesia conferred advantage, in terms of visual outcome. Rather, ultimate visual acuity was more directly related to the degree of initial injury. Finally, Fan et al reviewed visual outcomes of 507 OGI in which anesthesia mode (regional versus general) was left to the discretion of the attending anesthesiologist.[18] In this series 91% of patients were managed with a regional eye block, and post-operative improvements in visual acuity were similar for both groups. Fan et al concluded that, with judicious case selection, regional block and procedural sedation offer a viable alternative to GA for the repair of most open globe injuries.

High Flow Nasal Oxygen

Nowadays, there is a preference to perform ophthalmic surgeries at an ambulatory setting rather than traditional in-patient venues. Consequently, there is an increasing demand on anesthesiologists to accommodate all patients, even those with significant comorbidities.[19] This has resulted in some controversy because ASA III and IV status patients were formerly deemed inappropriate candidates for outpatient surgery. Patients with morbid obesity, advanced obstructive sleep apnea (OSA), respiratory compromise or potential for difficult airway were managed in centers with postoperative support facilities. However, recent trends have witnessed greater numbers of ASA III and IV patients undergoing surgery in ambulatory or office settings. This shift is, in some part, attributable to an increased availability and use of continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) devices in the peri-operative period. These devices promote improved oxygenation and ventilation in OSA or morbidly obese patients receiving monitored sedation and general anesthesia. Potential drawbacks of these devices include poor patient compliance, requirement for a leakproof mask fit, and compatibility with operating room equipment. In relation to ophthalmic

surgery, application of nasal CPAP or BiPAP via a sealed mask may afford improved respiratory mechanics without impairment of surgical access to the eye.[20]

High flow nasal oxygen (HFNO) devices offer an alternative therapy to CPAP. HFNO delivers oxygen, via nasal cannula, at flows anywhere between 10 and 70 liters / minute. The method is especially useful in obese patients because it maintains prolonged and satisfactory oxygen saturations regardless of spontaneous respiration or apnea. HFNO devices are easy to apply and better tolerated than CPAP because there is no requirement for a mask of unique design or obligation to attain an airtight seal. At higher flow rates the fractional inspired oxygen (FiO_2) approximates 100%. In addition, there is effective alveolar carbon dioxide washout and increased upper airway distending pressure resulting in an intrinsic CPAP effect.[21] Moreover, HFNO is more efficient at raising blood oxygen levels than conventional GA pre-oxygenation or nasal oxygen cannula used for procedural sedation.[22] Numerous studies describe preoxygenation at lower flow rates (10-40L/min), increasing to maximum flows of (60-70L/min) during GA induction. Prolongation of the safe apnea time has been documented in diverse patient populations, including the morbidly obese.[23] For example, HFNO decreases hypoxemic events during bronchoscopy, gastrointestinal, and endovascular procedures.[24-27] Additionally, HFNO is routinely employed as a definitive airway for GA-managed micro-laryngeal surgeries.[28] The proven efficacy of HFNO makes it an important tool in the management of difficult airways.[29,30]

There are no studies addressing the use of HFNO in ophthalmic surgery. In our experience, HFNO has been instrumental in three ways: 1) it is better tolerated than nasal CPAP 2) we use it frequently for morbidly obese and severe OSA patients and 3) it increases the margin of safety for high-risk patients during procedural sedation or GA management of the difficult airway. These factors have enabled us to care for patients previously deemed unsuitable at our ambulatory center. We believe further controlled studies examining the use of HFNO and nasal CPAP/BiPAP devices during ophthalmic surgery will contribute to improved safety.

Incision-free Sub-Tenon Anesthesia

Most adult eye surgeries are performed under regional or local anesthesia. In 1884, Turnbull published the first description of the sub-Tenon's block (STB) for ophthalmic anesthesia.[31] Later, in 1936, Atkinson coined the term 'retrobulbar anesthesia' for his needle-based technique that delivered local anesthetic behind the globe in proximity to the optic and ciliary nerves.[32] Subsequent technique modifications recognized that satisfactory ocular akinesia and surgical anesthesia were possible even when LA is deposited outside the extra-ocular muscle cone (peribulbar block). In recent decades, peribulbar anesthesia has superseded the retrobulbar technique because of lower complication rates. However, all needle approaches are infrequently associated with sight and life-threatening complications, such as brainstem anesthesia, retrobulbar hemorrhage and globe perforation. For this reason, Stevens revisited sub-Tenon anesthesia. In 1993 he described a technique of single quadrant injection using a blunt cannula.[33] The sub-Tenon approach has gained in popularity, especially in Europe and United Kingdom. Essentially, the efficacy of STB matches that of needle blockade. However, it is purported to lower the risk of major complications.[34-36]

Stevens' technique of sub-Tenon anesthesia necessitates incision of the conjunctiva and blunt scissor dissection to reach the sub-Tenon space and facilitate facile introduction of a curved cannula. While ophthalmologists are adept at globe interventions, many anesthesiologists are reticent to manipulate the eyeball. Consequently, cannula-based regional anesthesia became the domain of the ophthalmologist. Lately, the value of preemptive regional anesthesia performed in a holding area is recognized to offer great value in terms of quicker operating room turnover, cost savings and accelerated patient discharge. In 2006, Clarke et al conducted a prospective evaluation of STB success rates of two anesthesiologists.[37] Their learning curve was surprisingly flat because initial attempts were confounded by incomplete akinesia, chemosis and sub-conjunctival hemorrhage. However, both operators attained acceptable success rates after 60 blocks.

The requisite for a simple, non-surgical approach was answered by Allman. In 2008, he described an incision-free technique in which the conjunctiva is initially anesthetized with topical LA. Then, the inferior conjunctiva is raised and pierced using a blunt pencil point disposable tri-port cannula.[38] Thereafter, the cannula is advanced beneath the tenon capsule. Patient comfort may be accentuated by pre-application of a sterile, preservative-free lidocaine gel which allows for prolonged ocular surface contact time. Of interest, Aydin et al found that application of 2% and 5% lidocaine

ophthalmic gel inhibits growth of multiple organisms including *Candida albicans*.[39] Contemporary literature chronicles multiple modifications of Allman's technique. For example, Kumar and Seet describe an incision-free STB using a re-usable metal cannula, Palte and Gayer adopt a plastic disposable conjunctival probe, and Chua chronicled incision-free STB with a metal lacrimal dilator.[40-42] Following a limited preceptorship, Kilic reviewed her first experiences with incisionless STB for cataract and vitreoretinal surgery.[43] She reported satisfactory akinesia and anesthesia in 17 of 18 cases, suggesting proficiency is acquired sooner using incision-free techniques. These outcomes suggest that incision-free STB may be a more appropriate teaching tool for trainee anesthesiologists.

Dexmedetomidine

ADULT POPULATION

Dexmedetomidine is a selective, specific central alpha-2 agonist with sedative, anxiolytic, analgesic, and sympatholytic effects. A significant advantage is that it does not compromise oxygenation or ventilation. Originally investigated for sedation in the intensive care unit, it has now found uses in all facets of anesthetic care for both in-hospital and ambulatory patients. Dexmedetomidine may be administered either as a continuous infusion or intermittent bolus. Both routes produce onset of effect within 5 minutes and serum levels peak around 15 minutes. The elimination half-life of dexmedetomidine is approximately 2 hours. Dose dependent side effects include bradycardia, and initial hypertension followed by hypotension. Special caution should be taken when dexmedetomidine is administered to the elderly and patients receiving beta blocker therapy.[44,45]

Specifically, dexmedetomidine is being increasingly used as a sedative during ophthalmic surgery, and occasionally as an LA adjunct for eye blocks. Its efficacy for adult cataract surgery has been extensively studied. A recent meta-analysis demonstrated better analgesia, increased patient satisfaction, and decreased IOP when compared to traditional sedation regimens. However, these benefits must be weighed against cardiovascular depression and possible delayed recovery room discharge times.[46] A potential area for future investigation may be the role of dexmedetomidine in glaucoma surgery. A recent pilot study showed dexmedetomidine produced significant IOP reduction (33%) in patients with glaucoma with reversal of effect at two hours.[47] However, its use as a LA adjunct in order to lower IOP has met with mixed reviews.[48,49]

Our inclusion of dexmedetomidine in this commentary underscores its importance in changing our sedation regimen for many eye surgeries managed with an eye block and MAC. Our experience suggests that early administration of a dexmedetomidine bolus (8-20mcg) prior to midazolam (1-2mg) and/or low-dose fentanyl (0.5mcg/kg) produces ideal conditions for administration of peribulbar, retrobulbar, or sub-Tenon blocks. The inclusion of dexmedetomidine in our regimen has negated requirements for propofol administration, produces extended sedation and maintains adequate respiration without requirement for supplemental opioids and associated respiratory depression.

PEDIATRIC POPULATION

The use of dexmedetomidine in the pediatric population has been extensively studied particularly for the prevention of emergence delirium, a disordered state of consciousness in the post-operative period. Emergence delirium increases the risk for self-injury, delayed discharge, and need for additional nursing staff with associated increases in cost of care.[50] Intraoperative administration of dexmedetomidine via infusion or bolus is effective in mitigating emergence delirium and is now routinely administered for this purpose by many pediatric anesthesiologists.[51] A reduced incidence of emergence delirium has been specifically demonstrated in pediatric cataract and strabismus surgery.[52,53]

More recently, intranasal dexmedetomidine is being administered for premedication in pediatric patients. Doses of 1-4mcg/kg administered 30-45 minutes prior to induction are effective alternatives to oral midazolam.[54] The primary benefit of intranasal dexmedetomidine is predicta-ble sedation without respiratory depression. This makes dexmedetomidine an ideal premedication for children with obstructive sleep apnea or morbid obesity. In fact, comparative studies with midazolam attest to dexmedetomidine causing significantly fewer perioperative respiratory adverse events.[55] Disadvantages include latency of onset and prolonged duration of effect. Unfortunately, many ambulatory centers lack sufficient bed capacity to administer timely dexmedetomidine in advance of surgery, and this may account for documented cases of excessive post-operative drowsiness.

At our center we routinely use dexmedetomidine during all phases of pediatric care. Primarily, we administer intraoperative dexmedetomidine for the prevention of emergence delirium. Moreover, we use dexmedetomidine as an alternative in patients with a prior history of midazolam-induced delirium. We have met with success using dexmedetomidine for surgeries such as retinoblastoma, congenital glaucoma, and retinopathy of prematurity. In these patients, we have found early administration of intranasal dexmedetomidine is an effective sedative, and thereafter, children readily accept the mask for induction. Finally, parental feedback has been favorable especially for children with a history of untoward reaction to midazolam.

Conclusion

Recent improvements in surgical technique and ongoing technologic advancements affirm continued evolution of eye surgeries in terms of improved efficacy and lower invasiveness. In accommodating the expectations of all parties (surgeon, patient, and administration), anesthesia providers will need to assure patient comfort, rapid OR turnover, and early discharge without compromise of safety. Proficiency in regional ophthalmic anesthesia and monitored anesthesia care (with or without sedation) is key in meeting this goal. Management adaptations incorporating alternate medications, block techniques and modes of ventilation will assist in dismantling barriers that preclude surgery for ASA class III and IV at non-hospital venues.

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