

## Role of Adjuvants to Regional Anesthesia in Cataract Surgery

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### Abstract

The development of new medications and less intrusive procedures has expanded the range of anesthetic choices available for ocular surgery. In many ophthalmological procedures, regional anesthesia is now used instead of general anesthesia. This is because regional anesthesia is easier to administer, has a lower risk of serious systemic complications such as respiratory depression, circulatory collapse, or hypotension, and provides better pain relief after surgery. The single-injection peribulbar block seems to be the most suitable option for cataract surgery. Adjuvants are added to the peribulbar block to prolong its duration, which permits the method to be employed in lengthier operations, including vitreoretinal procedures, and gives better management of pain after surgery. In order to boost the strength and duration of local anesthesia and to minimize the time it takes for the anesthesia to take effect, additives have been utilized and tested in a variety of surgical procedures.

**Key words:** Ocular surgery, regional anesthesia, peribulbar block, adjuvants, pain management.

### Background

Cataract surgery is now a rapid and less intrusive process because to the development of new surgical methods and the availability of foldable intraocular lenses. As a result, the need for local anesthetic has also altered (1).

### Approaches to local anesthesia

Depending on the patient's profile and the kind of operation, intraocular surgery may be conducted under either regional anesthesia (such as ocular blocks) or general anesthesia. Using

blocks is helpful since it reduces the chances of problems in the heart and lungs, as well as postoperative nausea and vomiting (PONV). Furthermore, ocular blocks and topical anesthetic are linked to improved surgical pain relief and recovery, which results in a shorter hospital stay (2).

The objectives of ocular anesthesia for eye procedures include akinesia and anesthesia of the orbit (3).

### *Methods of Anesthesia*

#### **Topical Anesthesia**

Topical anesthetic is being utilized more and more in cataract surgery, particularly when combined with intracameral injection. For situations that are brief and straightforward and do not need total akinesia or regulation of IOP, topical anesthetic is a useful option. It is essential to choose the right patient since the patient has to stay motionless throughout the whole process. Regional or general anesthesia should be explored for patients who have low pain thresholds and significant levels of anxiety (4).

#### **Drugs**

When it comes to topical and injectable locoregional anesthesia, local anesthetic medicines may be selected from either the ester or the amide group, depending on the desired features. The structure, ionization and acidity, lipid solubility, protein-binding, and metabolism of LA medicines that are used topically and in blocks are all important properties. This may be accomplished by using eye drops (0.5% proparacaine, 0.5% tetracaine), gel (3.5% lidocaine), or sponges soaked with anesthetic. It is important to mention that adding subconjunctival lidocaine injection to topical anesthetic decreases postoperative discomfort and increases patient compliance during phacoemulsification (5).

#### **Regional Anesthesia**

When regional anesthesia is successful, it results in profound anesthesia and akinesia of the eye. During the regional block, standard monitoring should be used because rare complications such as oculocardiac reflex (OCR) (bradycardia or asystole), intravascular injection (systemic toxicity), or central nervous system injection (affecting the brainstem) may occur and require immediate intervention (6).

Midazolam may be used to sedate a patient, and low-dose remifentanyl can be given just before a regional block to decrease anxiety and minimize or eliminate discomfort during the

injection of the local anesthetic and the placement of the needle. Another method is to give the patient small amounts of propofol while the block is being performed. Because of the possibility of hypoxemia, supplemental oxygen (O<sub>2</sub>) is given during anesthesia for the block. Because the patient must be awake and cooperative throughout the surgery, long-acting medications should not be used. The combination of lidocaine (2%) and bupivacaine (0.75%) is the one that is utilized the most. Ropivacaine (0.75%) causes reduced discomfort during injection, provides good intraoperative akinesia, and is helpful for postoperative pain management. Hyaluronidase enzyme may be used as an adjuvant in local anesthetics at doses between 1 and 7.5 units/mL (7).

### *Methods*

There are several methods for administering injections to create anesthesia, including the retrobulbar, peribulbar, and sub-Tenon/conjunctival techniques (8).

### **Retro bulbar block (RBB)**

The Atkinson's or traditional retrobulbar block includes inserting a 38 mm long needle through the skin at the point where the medial two-thirds and lateral one-third of the inferior orbital edge meet in a rotated eye (which is tilted upwards and inwards). The needle is pointed toward the apex, and 2 ml of the anesthetic medication of your choosing (for example, lidocaine 2%) is administered. Typically, a supplementary facial nerve block (seventh nerve block CN VII) is utilized. The traditional retro bulbar block has been replaced with a larger volume contemporary intraconal (retro bulbar) block and a higher volume modern extra conal (peribulbar) block (9).

In the current retro bulbar block (Intraconal Block), a needle that is less than 31 mm long is intentionally pointed toward the apex and inside the muscle cone when the globe is in a neutral gaze (9).

### *Injection Method*

Eye drops with a topical local anesthetic and antiseptic (5% povidone iodine) are administered. A dilute local solution is created by adding 2 ml of concentrated local anesthetic agent to 13 ml and is beneficial before the main injection of concentrated local anesthetic agent. 1.5 to 2 ml of this dilute solution is injected via the conjunctiva, which is located under the inferior tarsal plate in the inferotemporal quadrant. A 27 gauge needle that is 1 cm long is placed via the conjunctiva and beneath the inferior tarsal plate in order to provide a diluted local anesthetic (4).

A 25 gauge or 27 gauge, 31 mm long needle is inserted through the skin or conjunctiva in the main inferotemporal quadrant as far lateral as possible (5 o'clock position on the right eye or

7 o'clock position on the left eye) below the lateral rectus muscle while the patient's eye is in the neutral gaze position. It is essential that the needle hub is always visible and that the skin does not get indented. The needle starts off by moving in a path that is tangential to the globe. It then moves below the globe and, after it has crossed the equator (as measured by the axial length of the globe), it is permitted to go upwards and inwards along the floor of the orbit. This allows it to reach the central space, which is located immediately behind the globe. The globe is constantly monitored while the needle is being placed. Before the surgery, it is necessary to do motility tests of the eye (9).

### *Drugs*

First should prepare either 0.4% oxybuprocaine HCl or 1% tetracaine for surface anesthesia, as well as 4 to 5 ml of the local anesthetic agent of your choice, which may be either 2% lidocaine or 0.5% bupivacaine. When optional adjunct medicines (hyaluronidase 15 IU/ml, epinephrine 1:200,000) are added to the local anesthetic, they generally increase diffusion and lead to a speedier onset. This creates excellent circumstances for eye surgery (10).

Akinesia and anesthesia often occur thereafter, however they depend on the dosage. If a modest dose is administered, anesthesia may ensue, but total akinesia may not happen. On the other hand, a bigger volume may typically assure anesthesia and akinesia, but it can also lead to an increase in intraocular pressure and other problems, such as chemosis (10).

Anesthesia and akinesia are both highly fast and predictable. If you have a basic understanding of the sciences that are related to block, it is simple to master the method (4).

### **Peribulbar block (PBB)**

The peribulbar block paralyzes the orbicularis oculi muscle, which improves the circumstances for performing ocular surgeries. This block reduces the chance of retro bulbar anesthesia, although in actuality, the dangers are about the same. PBB is just as effective as RBB, which shows that there is no anatomical barrier that prevents additional conal LA-deposits from diffusing into the intraconal area (11).

Peribulbar anesthesia may be administered by delivering the anesthetic agent at two distinct locations (Double injection approach). The first injection is given at the RBB injection site, and the second injection is given at the caruncle, which is located medially. Due to the danger of vascular injection and globe perforation, supero-nasal injections should be avoided (or performed more laterally). It may be manufactured using the single injection approach or Husted's

procedure at a single location. When peribulbar anesthesia is administered, a single site injection is less unpleasant than a double site injection. Compared to single site injection, double site injection has a higher risk of complications (12).

Medial Peribulbar Injection (also known as Medial Canthus or Caruncular Single Injection) When akinesia or anesthesia is insufficient, a medial peribulbar block is typically performed to supplement an inferotemporal retrobulbar or peribulbar injection. In this procedure, the needle is inserted into the blind pit between the caruncle and the medial canthus to a depth of 15 to 20 mm. The needle is placed at the medial side of caruncle, at the extreme medial side of the palpebral fissure and guided at a 5° angle away from the sagittal plane toward the medial orbital wall (3).

#### *Benefits of the Medial Peribulbar or Caruncular Technique*

Compared to double-injection peribulbar anesthesia, medial canthus single-injection peribulbar anesthesia is substantially less unpleasant and requires a less amount of anesthetic agent. The diffusion area of anesthetic drugs across the world is divided by a network of many small aponeuroses, which may be less dense in the medial canthus region. This might explain the improved diffusion and lower volume needed. This compartment has a rather substantial amount of extraconal space that is avascular, which may lower the chances of hematoma or intravascular injection (9).

#### **Sub-Tenon's Block**

Sub-Tenon anesthesia is a procedure that includes injecting a local anesthetic into the possible area that exists between the sclera and the Tenon capsule. According to Chua et al., the inferonasal conjunctival fornix is the most often used location for injections in order to prevent the insertion of the inferior oblique or medial rectus muscles. The treatment involves making a tiny cut in the sclera and then delicately inserting a cannula through that cut. After that, a local anesthetic is administered beneath Tenon's fascia, which surrounds the eye. This provides both pain relief and immobilization of the eye (13). Sub-Tenon anesthesia may be achieved using either anterior or posterior injection procedures. According to Xu et al. anterior injections are given superficially just beyond the equator using small amounts of anesthetic (3 to 5 ml) (14).

On the other hand, posterior injections provide a greater amount of anesthetic to the posterior intra- and extraconal areas. This means that fewer amounts of anesthetic may be used while still reducing the risk of chemosis (15).

### *Local anesthesia complications*

According to Upadhyay et al. (16), the local anesthetic procedures that are often employed in ocular operations are thought to be safe and dependable.

1. Hemorrhage in the retro bulbar and peribulbar regions: Retrobulbar and peribulbar bleeding are the most frequent complications that occur after periocular anesthetic injections. When a needle injures veins or tiny arteries, it creates modest hemorrhages that are often not dangerous to vision.

On the other hand, arterial hemorrhages may have catastrophic repercussions (17). If there is a tight orbit caused by fast enlargement of the orbit, prominent proptosis, chemosis, ecchymosis, blood-stained periorbital tissues, and high intraocular pressure (IOP), retro bulbar hemorrhage should be considered. The initial treatment is a lateral canthotomy with cantholysis or digital ocular compression, and the intraocular pressure (IOP) must be closely monitored. If the optic nerve is damaged, it may be essential to do an emergent orbital decompression. It is uncommon to hear of permanent vision loss as a result of hemorrhagic complications from periocular anesthetic. Once retrobulbar and peribulbar bleeding have been successfully managed, procedures may usually proceed (18).

2. Penetration, puncture, and rupture of the globe: The most serious needle injuries that may occur with periocular anesthetic are globe penetration, perforation, and rupture. If a needle is accidentally inserted into the globe, it may produce globe penetration (a single entrance wound) or globe perforation (entry and exit wounds). Globe rupture, also known as ocular explosion, occurs when there is a sudden increase in intraocular pressure (IOP) that causes the globe to explode. This may happen as a consequence of a direct injection of anesthetic into the eye. Myopia is a well-known risk factor for anesthetic needle injuries to the globe (19).

If a needle penetrates the eye, the signs and symptoms may include abrupt and intense pain, a loss or deepening of the red reflex, vitreous hemorrhage, hypotony, and impaired visual acuity. A globe rupture that is about to happen or is already happening may be indicated by the following alarming signs: the cornea becoming white, a significant rise in intraocular pressure, the eye getting bigger, the syringe plunger becoming more resistant to further advancement, and a popping sound being heard (2).

To assess a needle stick injury, a dilated fundal examination with an indirect ophthalmoscope should be conducted, followed by a B-scan to check for retinal detachment. The patient should then be quickly sent to a vitreoretinal specialist (20).

Retinal fractures and detachment, vitreous hemorrhage, macular disruption, macular epiretinal membrane development, subretinal hemorrhage, proliferative vitreoretinopathy, and optic nerve damage are all potential complications of globe penetration and perforations (21).

3. Damage to the optic nerve: If a needle is directly stuck into the optic nerve and central retinal vessels or if anesthetic is injected into the optic nerve sheath, it can have disastrous consequences. These consequences include optic nerve sheath hemorrhage, central retinal vessel occlusion, Purtscher's retinopathy, and brain-stem anesthesia. Improper anesthetic procedures and narrow orbits are also risk concerns. In periorbital blocks, needles longer than 35 mm should not be used, and all injections should be performed with the globe in the main gazing position. The results that were reported include photopsia during the injection, significant vision loss that cannot be explained, optic disc edema, retinal edema, and retinal or vitreous hemorrhage (2).

4. Injury to the extraocular muscles: Although it is uncommon for an anesthetic needle to injure the extraocular muscles, there have been a number of reports of instances in which patients who had no prior history of strabismus developed new eye misalignment and chronic diplopia after surgery (8).

5. Complications that may occur with sub-tenon anesthesia: The sub-tenon block (STB) technique reduces the chances of needle stick injuries during periorbital anesthesia. As a result, STB is seen to be a safer method than retro bulbar and peribulbar blocks. Although they are uncommon, there have been reports of sight-threatening consequences of STB, such as retro bulbar hemorrhage, globe perforation, muscle damage, and postoperative diplopia (13).

### **Additives to local anesthesia**

The complex system of connective tissue membranes dividing the orbital space has the potential to impede the spread of local anesthesia to reach the relevant motor and sensory nerves. There are a proportion of blocks that fail to provide adequate analgesia or akinesia. Therefore, various adjuncts to the local anesthetic fluid have been introduced to improve analgesia, akinesia, and duration of the anesthetic block (22).

### *Dexmedetomidine*

Dexmedetomidine has been used as an adjuvant in local anesthetic solution for various peripheral nerve blocks. Dexmedetomidine is a strong highly selective  $\alpha$ -2 adrenoreceptor agonist with an elimination half-life of 2 h. It possesses hypnotic, analgesic, and sympatholytic characteristics, and it promotes  $\alpha$ -2 selective vasoconstriction. Dexmedetomidine, acting on locus coeruleus, promotes drowsiness, anxiolysis, and near-natural sleep. Patients are still able to be awakened and had reduced muscular tone, lower intraocular pressure, less discomfort after surgery, and a lower need for opioids (23).

Delirium is linked to traditional sedative drugs, such as benzodiazepines, opioids, and propofol, because of the way they interact with gamma-amino butyric acid receptors. In individuals who have had non-cardiac surgery, dexmedetomidine decreases the occurrence of postoperative delirium (POD). It is not understood how dexmedetomidine works or how effective it is for reducing POD. Dexmedetomidine may be given by adding 50 mcg of dexmedetomidine to a combination of lidocaine 2% and bupivacaine in a single-injection percutaneous peribulbar anesthesia (24).

Dexmedetomidine is used during cataract surgery and results in a decrease in intraocular pressure (IOP), greater pain alleviation, and increased patient satisfaction. However, it also causes a comparatively greater amount of cardiovascular depression and a longer recovery discharge time. There were also reports of several variations in dosages, methods of administration, and outcome analysis in randomized controlled trials (RCTs) on dexmedetomidine. Therefore, dexmedetomidine should not be used routinely; it should only be considered in particular cases after thorough examination. Regardless of the technique employed, a smaller dosage should be administered in order to reduce the risk of negative side effects (25).

Dexmedetomidine may help minimize emerging agitation, postoperative nausea and vomiting, and postoperative pain, as well as decrease the incidence of oculocardiac reflex, in children strabismus surgery. Additionally, the length of time spent in the post-anesthesia care unit is not affected by the administration of dexmedetomidine (26).

When dexmedetomidine is administered, it often results in a decrease in blood pressure and heart rate, as well as cardiovascular depression. Patients who were given dexmedetomidine were shown to have improved breathing, as indicated by a lower end-tidal carbon dioxide (ETCO<sub>2</sub>) level and a higher respiratory rate. Jones and Aldwinckle conducted a systematic review and



found that there were no statistically significant differences in oxygen saturation, ETCO<sub>2</sub>, or respiratory rates in studies that compared dexmedetomidine with a placebo, midazolam, fentanyl, and propofol-alfentanil or ketamine-propofol combination (25).

In a systematic review, Jones and Aldwinckle presented bits of evidence that contradicted each other. Some research have claimed that dexmedetomidine leads to better analgesia and reduced pain perception during regional block; nevertheless, other investigations have demonstrated that there is no difference in analgesia and pain perception (25).

After cataract surgery, pain is usually thought to be mild (Rao and Rajan, 2021). According to a number of studies, there is no statistically significant difference in postoperative analgesia between dexmedetomidine and other medicines used in the research. After cataract surgery, ophthalmic regional anesthesia often offers enough or total pain relief (25).

Photic sneeze reflex, an autosomal dominant condition, involves sneezing in reaction to particular stimuli (e.g., staring at bright lights or periocular injection). According to Hakim and Alsaeid (27), combining propofol with fentanyl, dexmedetomidine, or antihistamines during the peribulbar block might decrease this response.

Intravenous dexmedetomidine has been demonstrated to significantly reduce intraocular pressure in a number of investigations. The decrease in intraocular pressure (IOP) that occurred during surgery with dexmedetomidine did not continue after the operation was over. This may be due to the medication's half-life of two hours, the brief length of cataract surgery, and the short amount of time that the drug was infused (25).

A comprehensive study has shown that patients treated with dexmedetomidine tend to take longer to recover, which raises questions about whether it is appropriate to use in outpatient surgical settings (25). In contrast, one research (C. M. Kumar et al., 2021) that compared dexmedetomidine (1 µg/kg over 10 minutes, followed by PCS at 5 µg bolus) with no sedation found no statistically significant changes in Aldrete scores 30 minutes following surgery (28).

### ***Midazolam***

Midazolam, is known to promote antinociception and increase the impact of local anesthetics used in neuraxial block. improved the benefits of the block by shortening the time it takes for anesthesia to begin and lengthening the duration of the analgesic effect. The addition of midazolam to the local anesthetic combination during peribulbar block for posterior segment surgery produced a more satisfying anesthetic result than the local anesthetic mixture alone (29).

It binds to the benzodiazepine receptor at the gamma-amino butyric acid (GABA) receptor, which increases the opening of chloride channels and membrane hyperpolarization. This produces a GABA-like inhibitory action on the central nervous system (CNS). Midazolam also has an effect on the reuptake of GABA, which causes it to build up at the synaptic cleft. Luckily, the typical therapeutic dosages of neuraxial midazolam do not cause any negative side effects (30).

The peripheral target is thought to be the translocator protein (TSPO), which was formerly referred to be the peripheral benzodiazepine receptor. TSPO is a cholesterol binding protein that is located in the outer mitochondrial membrane throughout the body, where it is involved in the generation of steroids. Additionally, it has been shown that it has a protective effect in microglial cells after nerve injury (31).

Midazolam is different from other benzodiazepines in that it has a quicker onset, is more potent, has a higher metabolic clearance, and is water-soluble. These characteristics reduce the risk of local adverse effects after injection. While there are worries about neurotoxicity in animal models when midazolam is administered intrathecally and epidurally, there have been no adverse effects in humans when therapeutic dosages of the medication are given neuraxially. Multiple findings indicate that it is safe to use in a variety of surgical operations (32).

Midazolam is nearly entirely metabolized to its hydroxyl metabolites by CYP3A4. Midazolam levels may be influenced by substances that either induce or inhibit CYP3A4. Drugs such glucocorticoids, antifungals, antibiotics, retrovirals, antidepressants, calcium channel blockers, and H2 blockers interact with each other to affect the way midazolam is disposed of (33).

When there is acute or chronic inflammation, proinflammatory cytokines such as interleukin (IL)-1 $\beta$ , tumor necrosis factor (TNF)- $\alpha$ , and IL-6 are released. These cytokines act as signaling molecules, causing significant changes in the expression profiles of liver genes and resulting in a strong downregulation and reduction in the activity of many drug-metabolizing enzymes, including CYP3A4 (34).

In critically sick patients with acute inflammation, midazolam clearance was shown to be linked to plasma levels of the inflammatory marker C-reactive protein. In patients with severe inflammatory syndrome caused by acute respiratory syndrome-coronavirus 2, an increase in C-reactive protein was strongly linked to a reduction in the 1-OH-M/midazolam plasma ratio. This suggests that CYP3A is less able to metabolize midazolam (11).

## References

1. Bedrossian Edward H. J. The Orbit: Lateral Approach [Internet]. Anatomy of the Eyelid, Orbit, and Lacrimal System. Springer International Publishing; 2022. p. 51–8. Available from: [http://dx.doi.org/10.1007/978-3-030-88265-5\\_6](http://dx.doi.org/10.1007/978-3-030-88265-5_6)
2. Singh RB, Khera T, Ly V, Saini C, Cho W, Shergill S, et al. Ocular complications of perioperative anesthesia: a review. Graefe's Arch Clin Exp Ophthalmol [Internet]. 2021;259(8):2069–83. Available from: <http://dx.doi.org/10.1007/s00417-021-05119-x>
3. Goyal N. Head and Neck: Retrobulbar Block and Peribulbar Block [Internet]. Anesthesiology In-Training Exam Review. Springer International Publishing; 2022. p. 175–8. Available from: [http://dx.doi.org/10.1007/978-3-030-87266-3\\_34](http://dx.doi.org/10.1007/978-3-030-87266-3_34)
4. Sahutoglu C. Anesthesia for ophthalmic surgery. Eur Eye Res [Internet]. 2024;90–102. Available from: <http://dx.doi.org/10.14744/eer.2023.44127>
5. Wutthayakorn W, Chansangpetch S, Tunruttanakul S. Topical and subconjunctival anesthesia versus topical anesthesia alone in patients with senile cataracts undergoing phacoemulsification: a double-blind randomized controlled trial. BMC Ophthalmol [Internet]. 2024;24(1):20. Available from: <https://pubmed.ncbi.nlm.nih.gov/38216983>
6. Klein AA, Meek T, Allcock E, Cook TM, Mincher N, Morris C, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2021. Anaesthesia [Internet]. 2021;76(9):1212–23. Available from: <http://dx.doi.org/10.1111/anae.15501>
7. Taylor A, McLeod G. Basic pharmacology of local anaesthetics. BJA Educ [Internet]. 2019/12/04. 2020;20(2):34–41. Available from: <https://pubmed.ncbi.nlm.nih.gov/33456928>
8. Scholle TM. Anesthesia for Ocular Surgery. Int Ophthalmol Clin [Internet]. 2020;60(4):41–60. Available from: <http://dx.doi.org/10.1097/iio.0000000000000337>
9. van Zundert A, Kumar C, Jankovic D. Regional Anesthesia in Ophthalmology [Internet]. Regional Nerve Blocks in Anesthesia and Pain Therapy. Springer International Publishing; 2022. p. 87–104. Available from: [http://dx.doi.org/10.1007/978-3-030-88727-8\\_6](http://dx.doi.org/10.1007/978-3-030-88727-8_6)
10. Naguib NN, Mohasseb TM, Ezzat AM, Hussien GZ, Khattab RS, Aboul Fetouh ES, et al. Ultrasound-guided versus conventional peribulbar anaesthesia in cataract surgery: A randomised controlled study. J Perioper Pract [Internet]. 2022;33(10):302–7. Available from: <http://dx.doi.org/10.1177/17504589221117670>
11. Le Carpentier EC, Canet E, Masson D, Martin M, Deslandes G, Gaultier A, et al. Impact of Inflammation on Midazolam Metabolism in Severe COVID-19 Patients. Clin Pharmacol Ther [Internet]. 2022/07/27. 2022;112(5):1033–9. Available from: <https://pubmed.ncbi.nlm.nih.gov/35776074>
12. Babu N, Kumar J, Kohli P, Ahuja A, Shah P, Ramasamy K. Clinical Presentation and Management of Eyes with Globe Perforation during Peribulbar and Retrobulbar Anesthesia: A Retrospective Case Series. Korean J

- Ophthalmol [Internet]. 2021/11/08. 2022;36(1):16–25. Available from: <https://pubmed.ncbi.nlm.nih.gov/34743491>
13. Chua MJ, Lersch F, Chua AWY, Kumar CM, Eke T. Sub-Tenon's anaesthesia for modern eye surgery-clinicians' perspective, 30 years after re-introduction. *Eye (Lond)* [Internet]. 2021/02/03. 2021;35(5):1295–304. Available from: <https://pubmed.ncbi.nlm.nih.gov/33536591>
  14. Xu Q, Ren M, Guan J, Shi G, Ni Y, Luan J. Efficacy and safety of trans-sub-Tenon's retrobulbar anesthesia for pars plana vitrectomy: a randomized trial. *BMC Ophthalmol* [Internet]. 2022;22(1):289. Available from: <https://pubmed.ncbi.nlm.nih.gov/35773662>
  15. A. Sherif N, Mohamad MK, Hannon AA, Osama NA. A Comparative Study Between Single Medial Canthus Injection Using 13 x 0.45 mm Needle and Posterior Sub-Tenon Injection as Local Anesthesia Techniques for Strabismus Surgery in Adults. *Open Anesth J* [Internet]. 2020;14(1):8–13. Available from: <http://dx.doi.org/10.2174/2589645802014010008>
  16. Upadhyay P, Ichhpujani P, Solanki A. Recent trends in anesthetic agents and techniques for ophthalmic anesthesia. *J Anaesthesiol Clin Pharmacol* [Internet]. 2022/07/13. 2023;39(3):343–8. Available from: <https://pubmed.ncbi.nlm.nih.gov/38025549>
  17. Periasamy S, Srinivasan S, Damodharan G. Assessment of complications of peribulbar block in patients undergoing cataract surgery in tertiary care center – A record-based observational study. *TNOA J Ophthalmic Sci Res* [Internet]. 2021;59(4):354. Available from: [http://dx.doi.org/10.4103/tjosr.tjosr\\_84\\_21](http://dx.doi.org/10.4103/tjosr.tjosr_84_21)
  18. Kim JH, Hayashi S, Yamamoto M, Murakami G, Wilting J, Rodríguez-Vázquez JF. Examination of the Annular Tendon (Annulus of Zinn) as a Common Origin of the Extraocular Rectus Muscles: 2. Embryological Basis of Extraocular Muscles Anomalies. *Invest Ophthalmol Vis Sci* [Internet]. 2020;61(12):5. Available from: <https://pubmed.ncbi.nlm.nih.gov/33026455>
  19. Kumar A, Kakkar P, Agarwal D, Kumar A. Needle Stick Globe Injuries [Internet]. *Posterior Segment Complications of Cataract Surgery*. Springer Singapore; 2020. p. 11–5. Available from: [http://dx.doi.org/10.1007/978-981-15-1019-9\\_2](http://dx.doi.org/10.1007/978-981-15-1019-9_2)
  20. Skidmore C, Saurey T, Ferre RM, Rodriguez-Brizuela R, Spaulding J, Lundgreen Mason N. A Narrative Review of Common Uses of Ophthalmic Ultrasound in Emergency Medicine. *J Emerg Med* [Internet]. 2021;60(1):80–9. Available from: <http://dx.doi.org/10.1016/j.jemermed.2020.08.003>
  21. Datta D, Khan P. Medial canthal peribulbar block — a safe, efficacious alternative to conventional peribulbar block. *Ophthalmol J* [Internet]. 2023;8(0):131–7. Available from: <http://dx.doi.org/10.5603/oj.94021>
  22. Mohankumar A, Rajan M. Role of hyaluronidase as an adjuvant in local anesthesia for cataract surgery. *Indian J Ophthalmol* [Internet]. 2023;71(7):2649–55. Available from: <https://pubmed.ncbi.nlm.nih.gov/37417102>
  23. Jean Y-K, Kam D, Gayer S, Palte HD, Stein ALS. Regional Anesthesia for Pediatric Ophthalmic Surgery: A Review of the Literature. *Anesth & Analg* [Internet]. 2020;130(5):1351–63. Available from:

- <http://dx.doi.org/10.1213/ane.0000000000004012>
24. M. AA, Mohammad NA, Maghawry KM, Elderh MS, AbdulAziz MM. Dexmedetomidine versus magnesium sulphate as an adjuvant to local anesthesia in single-injection percutaneous peribulbar anesthesia for cataract extraction. *Ain-Shams J Anesthesiol* [Internet]. 2021;13(1). Available from: <http://dx.doi.org/10.1186/s42077-021-00191-1>
  25. Jones JH, Aldwinckle R. Perioperative Dexmedetomidine for outpatient cataract surgery: a systematic review. *BMC Anesthesiol* [Internet]. 2020;20(1):75. Available from: <https://pubmed.ncbi.nlm.nih.gov/32247310>
  26. Chouhan S. Day Care Anaesthesia in Ophthalmic Procedures [Internet]. *Anesthesia in Day Care Surgery*. Springer Singapore; 2019. p. 81–9. Available from: [http://dx.doi.org/10.1007/978-981-13-0959-5\\_13](http://dx.doi.org/10.1007/978-981-13-0959-5_13)
  27. Hakim KY, Alsaied MA. Comparative Study between the Efficacy of Fentanyl, Antihistamines, and Dexmedetomidine in Suppressing Photic Sneeze Reflex during Peribulbar Block. *Anesth essays Res* [Internet]. 2019;13(1):40–3. Available from: <https://pubmed.ncbi.nlm.nih.gov/31031478>
  28. Kumar R, . A, Das AK, Verma NK, Saxena AC, Hoque M. Systemic effects and clinical application of dexmedetomidine. *Pharma Innov* [Internet]. 2020;9(11):241–6. Available from: <http://dx.doi.org/10.22271/tpi.2020.v9.i11d.5344>
  29. Abdalla Mohamed A, Safan TF. Fentanyl versus midazolam as additive to local anesthetic mixture for peribulbar block during posterior segment surgery in adult patients a prospective randomized double-blind study. *Ain-Shams J Anesthesiol* [Internet]. 2019;11(1). Available from: <http://dx.doi.org/10.1186/s42077-019-0036-8>
  30. Vats A, Marbaniang MJ. The principles and conduct of anaesthesia. *Surg* [Internet]. 2022;40(6):361–9. Available from: <http://dx.doi.org/10.1016/j.mpsur.2022.04.002>
  31. Prabhakar A, Lambert T, Kaye RJ, Gagnard SM, Ragusa J, Wheat S, et al. Adjuvants in clinical regional anesthesia practice: A comprehensive review. *Best Pract & Res Clin Anaesthesiol* [Internet]. 2019;33(4):415–23. Available from: <http://dx.doi.org/10.1016/j.bpa.2019.06.001>
  32. Osama NA, Mohamed MK, Fetouh ISA, Sherif NA. Ketamine versus midazolam as an adjuvant to peribulbar block using a single inferonasal injection in patients undergoing vitreoretinal surgery: A randomized controlled trial. *Rev Española Anesthesiol y Reanim (English Ed)*. 2023;70(5):276–83.
  33. Denisov IG, Grinkova Y V, McLean MA, Camp T, Sligar SG. Midazolam as a Probe for Heterotropic Drug-Drug Interactions Mediated by CYP3A4. *Biomolecules* [Internet]. 2022;12(6):853. Available from: <https://pubmed.ncbi.nlm.nih.gov/35740978>
  34. Buja A, Miatton A, Cozzolino C, Monasta L, Grada A, Karimkhani CA, et al. The global, regional, and national burden of seborrheic dermatitis: results and insights from the Global Burden of Disease 2019 Study. *Arch Dermatol Res* [Internet]. 2022; Available from: <http://dx.doi.org/10.1007/s00403-022-02469-2>