Egyptian Journal of Medical Research

Print ISSN: 2682-4396 / Online ISSN: 2682-440X

Original article

Comparative randomized double-blind study between Neostigmine and Dexmedetomidine as additives to local anethetic mixture in peribulbar anesthesia In cataract operations.

Ahmed Goda Ahmed [a], Mahmoud Attia Ali[a], Dina yahia kassim[a] , Mai Samir Ibrahim Fahmy Darwish[a] , Hazem Abdelwahab Hussein[a]

[a] *Anesthesiology, surgical intensive care and pain management Faculty of Medicine, Beni-Suef University, Egypt.*

Article Info

Article history:

Received 6 December 2022

Accepted 14 December 2022

Corresponding Author:

Mai Samir Ibrahim

maisamir385@gmail.com

Keywords:

Dexmedetomidine

Neostigmine

Peribulbar

anesthesia

Abstract

Background: Local anesthetics are commonly injected into the peribulbar space. However, utilizing solely local anesthetics is linked to delayed initiation of globe akinesia, shorter duration of analgesia, and frequent replenishment with block. This research aimed to evaluate the peribulbar anesthetic effects of neostigmine and dexmedetomidine to those of a local anesthetic combination. **Methods:** The current study was conducted in Beni-Suef University Hospital on 72 patients. The patients were divided randomly into two equal groups: Dexmedetomidine group included 36 patients who received 50-µg dexmedetomidine added to local anesthetics mixture and neostigmine group included 36

patients who received 0.5 mg of neostigmine added to local anesthetics mixture. **Results:** There was a significantly longer duration till the onset of block in neostigmine groups than dexmedetomidine group. The initiation of motor and sensory block reached an average of 2.5±0.9 minutes in dexmedetomidine group while in neostigmine group the mean time was 3.9±1.2 minute. **Conclusions:** This research revealed that adding 50 µg of dexmedetomidine or 0.5 mg of neostigmine to the local anesthetic mix in peribulbar anesthesia for surgery of cataract enhanced the onset of motor and sensory blocks of the globe and prolonged the duration of the block. Dexmedetomidine was better than neostigmine in faster onset of block, prolonged duration, low dose of local anesthetic needed.

1. Introduction:

Since older patients who are eligible for ocular procedures often have various systemic disorders that make them more prone to anesthetic problems, regional anesthesia is the preferred method of anesthesia for eye surgery due to its many benefits (1).

Regional anesthetic also has the added benefit of reducing the likelihood of postoperative nausea and vomiting by blocking the endocrine and metabolic reaction to the procedure (2).

Retrobulbar anesthesia has been linked to an increased risk of complications as brainstem anesthesia, globe perforation, and retrobulbar hemorrhages (3).

Parasympathomimetic drugs like neostigmine work by binding to the active location of acetylcholine esterase enzyme, and prevent it from hydrolyzing acetylcholine molecules. This results in an increased level of acetylcholine at peripheral muscarinic receptors present in the peripheral nerve ending, which in turn activates the cholinergic-mediated

antinociception by activating the No-cGMP pathway, thereby extending (4).

Researchers have looked at the pain-relieving benefits of neostigmine when it is injected peripherally, such as during intravenous regional anesthesia, intraarticular injections, or an axillary block. According to their findings, when neostigmine was added to the local anesthetic solution, it sped up the onset of anesthesia, lengthened its duration, and increased the time before the first analgesic request was made (5).

Dexmedetomidine is an alpha2-adrenoceptor agonist with eight times the affinity of clonidine. When given intravenously to healthy volunteers or postoperative ICU patients, dexmedetomidine has been demonstrated to have sedative, analgesic, and anxiolytic effects. Administered in conjunction with local anesthetics, dexmedetomidine has shown effective for peripheral nerve block, brachial plexus block, and intrathecal anesthesia (6,7).

The aim of this research was to evaluate the effect of addition of neostigmine and dexmedetomidine to a local anesthetic combination in a peribulbar block and comparing the results to those obtained with only the block as a primary outcome. The secondary outcomes were to assess the quality of surgical circumstances, patient satisfaction, length of sensory and motor block, amount of local anesthetic utilized, and time before first analgesic request. Moreover, the side effects as bradycardia, nausea, vomiting, and stomach cramps were assessed.

2. Patients and Methods:

This research was implemented between October 2021 and March 2022 at the department of anesthesiology, surgical critical care, and pain management at Beni-Suef University.

There were 72 individuals of both sexes included in this study. They were assigned randomly into one of two treatment groups using sealed opaque numbered envelopes identifying the group each patient belonged to. The study medication was manufactured in identical syringes with the word "research drug" written on them, and the anesthesia residents who were in charge of administering and collecting data during general anesthesia were also blinded to the study's procedure. Each patient was randomly allocated to one of two groups (36 patients each). Patients in Group I were given a combination of bupivacaine 0.5%

(4ml), lidocaine 2% (4.5 ml), dexmedetomidine 50 µg (1 ml), and hyaluronidase hydrochloride 2% (90 IU) in a saline solution (the total volume is 9ml in 10ml syringe). Anesthetic solution for Group II was 9 ml in a 10 ml syringe and included 4 ml of isobaric bupivacaine, 5%, 4.5 ml of lidocaine hydrochloride, 2%, including 90 IU of hyaluronidase, and 1 ml (0.5 mg) of neostigmine.

Inclusion criteria:

Seventy-two patients ASA physical status I or II aged from 55 to 75 years scheduled for cataract surgery operation under peribulbar anesthesia.

Exclusion criteria:

Patients with any of the following criteria coagulopathy or taking anticoagulants, infection at block site, axial length larger than 26 mm, or posterior staphyloma, local anesthesia sensitivity, refusal of treatment or inability to take a decision as deafness or mentally retarded, medical condition prevent peripheral nerve blockade, bronchial asthma, brady arrhythmias, and presence of severe systemic disease.

Anesthetic Technique:

The trial only enrolled patients with an ASA score of I or II, and every patient underwent a preoperative evaluation that comprised a medical history, physical exam, and routine tests.

The local anesthetic solution was prepared in similarly sized syringes by an anesthesiologist who was not engaged in the research so that neither the patients nor the anesthesiologist knew what was in it. All patients were administered 150 mg of oral ranitidine the morning of the procedure following a 6-hour fast.

During the intervention, a twenty-two-gauge cannula was put in the dorsum of non-dominant hand then a multi-channel monitor was connected to the patient (Hewlett packward, viridian 24 germany) that captured the patient's blood pressure, oxygen saturation, heart rate, and ECG (spo2). The patients were positioned supine and given nasal cannulas to deliver 3 liters of oxygen per minute. The syringe containing the anesthetic solution has a (25 gauge), 25 mm long needle connected to it for injection.

The patients were lying supine with their gaze fixed on a point on the ceiling. After sterilizing the lower eyelid, the anesthesiologist pushed the eyeball up with their non-dominant hand and inserted the needle 1-1.5 cm medial to the lateral canthus

on the inferior eyelid, angling it slightly medially (25 degrees) and cephalad (15 degrees) until the needle's hub touched the skin.

After doing a negative aspiration, the appropriate local anesthetic mix was delivered to the patient's eyes without crowding. Gentle, intermittent pressure was applied to the eye for 5 minutes after the injection to lower intraocular pressure, help in the dispersion of the anesthetic composition, and elicit akinesia of the periorbital muscles.

Assessment parameters and follow up:

Hemodynamic measurements, such as cardiac rate, noninvasive blood pressure, and oxygen saturation. To assess how long it took for the cornea to become entirely unresponsive to touch after injection, researchers gently touched the corneas of test participants with a cotton swab and then measured the elapsed time in minutes. Initiation and timing of eyeball motor obstruction (globe akinesia). The surgeon's assessment of the patient's condition after surgery.

On a visual analog scale, the period between when the local anesthetic was fully administered and when the patient first sought pain medicine.

The neostigmine drug related side effects as bradycardia, bronchospasm, increased salivation, nausea, vomiting, diarrhea, and colic or the dexmedetomidine related side effects as low blood pressure, fever, high blood pressure, anemia, vomiting, and tachycardia. In addition to the side effects of the technique itself as brain stem anesthesia, globe perforation, retrobulbar hemorrhage. Assessment of Intra ocular pressure (IOP) postoperatively.

After surgery, patients were sent to the post-anesthesia care unit (PACU) to recover from the anesthesia and be assessed before being transferred to the normal ward.

Data analysis and statistics:

The Pearson Chi-square test for independence of attributes/exact Fisher's test was applied to compare the two groups based on the categorical variables represented as numbers of patients and percentages of patients. The Mann-Whitney U-test was applied to do group comparisons based on continuous variables reported as mean, median, and standard deviation. For this study, we utilized SPSS 20 (IBM) and set our alpha at 5%, therefore results with a P value of less than 0.05 were deemed significant.

Ethical considerations:

Before beginning the study, the research ethics committee of Beni-Suef University's medical school gave its approval with number FMBSUREC/05122021/Darwish. A written informed consent was obtained from all subjects. Patients had a full right to refuse participation without affecting the medical care expected to be offered to the patient. All data was confidential and anonymous.

3. Results:

Patients' age and sex in both groups were matched. The mean age in Dexmedetomidine group was 52.6±4.3 years and in Neostigmine group was 49.6±10.2 years **(table 1).**

Table (1): Baseline characteristics of the studied groups.

Items	Dexmedetomidine group (no=36)	Neostigmine group (no=36)	P-value
Age (mean±SD)	52.6±4.3	49.6±10.2	0.118
Sex Males Females	 16(44.4%) 20(55.6%)	 15(41.7%) 21(58.3%)	 0.812

Table (2) showed that there was a significant longer duration till the onset of block in neostigmine groups than Dexmedetomidine group (P-value<0.001).

TPrimary: Comparison between the studied groups regarding the onset of sensory and motor block (primary outcome).

Items	Dexmedetomidine group (no=36)	Neostigmine group (no=36)	P-value
Onset of block in minutes (mean±SD)	2.5±0.9	3.9±1.2	<0.001* (MW)

**P-value is significant* *MW: Mann Whitney U test*

There was a significant higher dose of anesthesia in neostigmine groups than Dexmedetomidine group (P-value<0.05). All patients in both arms were satisfied and both arms had a qualified surgical field. The duration block in both arms didn't differ significantly **(table 3).**

Table (3): Comparison between the studied groups regarding the Duration of sensory and motor block, need for block supplementation, volume of local anesthetic used, 1st analgesic request, satisfaction of the patients, quality of operative conditions (secondary outcome).

Items	Dexmedetomidine group (no=36)	Neostigmine group (no=36)	P-value
Duration of block (hour)	2.5±0.9	2.3±0.6	0.164
Need for block supplementation	0(0.0%)	1(2.8%) (2cm)	>0.999 (FET)
Volume of local anesthetic used (cm)	6.4±0.9	7.1±1.3	0.006* (MW)
Analgesic request	0(0%)	0(0%)	---
Satisfaction of the patients	36(100%)	36(100%)	----
Quality of operative conditions	36(100%)	36(100%)	----

**P-value is significant. MW: Mann Whitney U test FET: Fisher Exact test*

There was no significant difference between neostigmine groups than Dexmedetomidine group regarding the occurrence of complications (P-value>0.05). All patients in both had no post-operative diarrhea or vomiting **(table 4).**

Table (4): Comparison between the studied groups regarding the occurrence of complications.

Items	Dexmedetomidine group (no=36)	Neostigmine group (no=36)	P-value
Bradycardia	0(0.0%)	1(2.8%)	>0.999 (FET)
Abdominal cramps	0(0.0%)	1(2.8%)	>0.999 (FET)
Diarrhea/vomiting	0(0.0%)	0(0.0%)	---

FET: Fisher Exact test

Table (5) showed that there was no significant difference between neostigmine groups than Dexmedetomidine group regarding the post-local intraocular pressure (P-value>0.05).

Table (5): Comparison between the studied groups regarding the post-local intraocular pressure.

Items	Dexmedetomidine group (no=36)	Neostigmine group (no=36)	P-value
IOP (mean±SD)	15.1±0.8	14.8±0.9	0.097

Table (6) showed that there was no significant difference between neostigmine groups than Dexmedetomidine group regarding the post operative blood pressure, heart rate and SO2 (P-value>0.05).

Table (6): Comparison between the studied groups regarding the post-operative blood pressure, heart rate and SO2.

Items (mean±SD)	Dexmedetomidine group (no=36)	Neostigmine group (no=36)	P-value
SBP	130.8±11.3	136.7±16.7	0.087
DBP	84.7±6.5	83.1±8.6	0.364
HR	77±8	79±10	0.328
SO2	98.2±1.1	98.1±1.1	0.828

SBP: systolic blood pressure DBP: diastolic blood pressure HR: heart rate SO2: saturation of oxygen

4. Discussion:

As a result, most anterior and posterior segment intraocular procedures are now performed under local anesthesia rather than general anesthesia. For eye procedures, LA is administered in the form of retrobulbar, peribulbar, and sub-blocks, Tenon's all of which induce akinesia and provide anesthesia (8). As it is a straightforward and safe approach that results in good analgesia and akinesia of the eye, peribulbar block is the most popular regional anesthetic technique used globally to give anesthesia

for Cataract Extraction and Intra Ocular Lens Implantation (CE and IOLI) (9).

In order to speed up the onset of block and improve anesthesia quality and duration, several adjuvants have been used with local anesthetic solutions in various regional anesthesia procedures (Sherif et al., 2019).

This research looked at peri-bulbar anesthesia using neostigmine and dexmedetomidine added to the local anesthetic. Patients in the dexmedetomidine group had an average age of 52.6±4.3 and were mostly female (55.6 percent). Patients in the neostigmine group had a mean age of 49.6±10.2, and the majority of them were female (58.3 percent). In terms of age and sex distribution, neither group differed significantly from the other.

Our study showed that there was a significantly longer duration till the onset of block in neostigmine groups than dexmedetomidine group. The onset of motor and sensory block reached an average of 2.5±0.9 minutes in dexmedetomidine group while in neostigmine group the mean time was 3.9±1.2 minute.

Abd Elmoniem and Kamel, (2019) found a similar outcome when they examined the additive impact of dexmedetomidine and magnesium sulphate to local anaesthesia of peribulbar block in cataract surgery. They found that the dexmedetomidine group had a quicker onset of sensory block and globe akinesia. Both sensory block (2.05±0.65 min) and globe akinesia (2.9±1.1 min) began at around the same time (11).

Dexmedetomidine's adjuvant impact to local anesthetic combination in peribulbar block for eye procedures has been studied extensively. Our findings were supported by the research of Fayed et al. (2018), who examined the impact of adding dexmedetomidine to the local anesthetic combination in peribulbar block. They demonstrated that adding 25 micrograms of dexmedetomidine to a peribulbar block significantly increased the duration of sensory and motor akinesia and sped up the onset of corneal anaesthesia and globe akinesia (12).

When added to a combination for peribulbar anesthesia in vitreoretinal operations, Hafez et al. (2016) discovered that dexmedetomidine sped up the start of sensory and motor block and lengthened its duration and the analgesia period (13)

Adding magnesium sulphate and dexmedetomidine to a local anesthetic

demonstrated a statistically significant difference between groups, as determined by a study by Kassem et al., 2018. The block started happening faster in the dexmedetomidine group than in the magnesium sulphate group or the placebo group (14).

The effects of adding 50 µg and 25 µg of dexmedetomidine to peribulbar block in conjunction with local anesthetic were studied by Channabasappa et al., 2013. Compared to the control group, individuals who received 50 micrograms of dexmedetomidine had a much quicker start of corneal anaesthetic and globe akinesia (15).

Dexmedetomidine's ability to act as a strong and selective agonist of central alpha-2 adrenergic receptors may account for this effect. Despite its lack of respiratory-sparing properties, this adjuvant has been shown to be beneficial in lowering the requirement for opioids in the perioperative phase and may even result in cooperative sedation when administered in a variety of ways (16).

When used with a local anesthetic, dexmedetomidine acts as an adjuvant to improve the quality of anesthesia and postoperative analgesia by increasing central and peripheral neural blockades (17).

By inhibiting cholinesterase, neostigmine boosts acetylcholine levels in nerve endings. This action is achieved by the retention of acetylcholine at the nerve terminal by competitive binding at the active site of acetylcholinesterase (18).

The effects of neostigmine as an adjunct to local anesthesia for eye procedures have been the subject of little research. Similar findings were found in the research by Aboul Fetouh et al., (2021) on the adjuvant impact of various dosages of neostigmine to local anesthesia of the eye, which revealed that neostigmine at 0.5 mg accelerated the onset of motor and sensory block (19).

It is believed that neostigmine's potential as an adjuvant is not due to its impact on endplates containing nicotinic receptors, but rather to its function to enhance acetylcholine at muscarinic junctions of peripheral neurons. Cholinesterase inhibitors have a dose-dependent impact on the activation of intrinsic ascending and descending cholinergic pathways (20).

All patients in both groups reported feeling comfortable under anesthesia, and all groups provided competent surgical fields for the

surgeons. In the dexmedetomidine group, the average block lasted for 2.5±0.9 hours, whereas in the neostigmine group, it lasted for 2.3±0.6 hours, hence there was no statistically significant difference between the two groups. The neostigmine group received a much greater dosage of anesthetic than the dexmedetomidine group. Average local anesthetic volume was 7.1±1.3 cm in the neostigmine group and 6.4±0.9 cm in the dexmedetomidine group.

Abd Elmoniem and Kamel's (2019) research on peribulbar anesthesia demonstrated that improving the quality of operative conditions by adding dexmedetomidine to the local anesthetic mixture increased patient and doctor satisfaction and increased the length of time the block lasted without causing any serious adverse effects (20).

Furthermore, Fayed et al. (2018) found that adding 25 g dexmedetomidine to the local anesthetic combination in peribulbar block significantly increased patient and surgeon satisfaction with the duration of sensory and motor akinesia (12).

Concerning neostigmine, Aboul Fetouh et al., (2021) showed that patients and surgeons were content with the addition of neostigmine to the local anesthetic mixture in peribulbar block since it offered the drowsiness that allowed complete collaboration (19).

In addition, previous study illustrated that the time to first postoperative rescue analgesia and duration of sensory and motor block were all improved when neostigmine was added to peripheral nerve blocks during upper limb surgery (22).

As regards the postoperative complications, there was no significant difference between both groups regarding the occurrence of complications. All patients in both groups had no post-operative diarrhea or vomiting. Only one patient in the neostigmine group had bradycardia and one patient had abdominal cramps.

This result agrees with previous research that stated that combining a local anesthetic with dexmedetomidine produces profound drowsiness without resulting in respiratory depression. Sedation with dexmedetomidine allows for optimal surgical circumstances, patient participation, and little risk of complications (23). In addition, the analgesic effectiveness and safety of adding 25 µg neostigmine to 20 mg bupivacaine during spinal anesthesia for lower limb orthopedic surgery was studied by Kayalha

et al., 2015. The researchers found no association between neostigmine and adverse events (24).

Bradycardia is explained by the parasympathetic nervous system activation by neostigmine causing its most prevalent adverse effects, including bradycardia, hypotension, and postoperative nausea and vomiting (25).

A greater dosage (750-1 mcg) of the medication neostigmine was used initially, however this caused nausea and vomiting, thus lower levels were advised (26).

Mean post-local intraocular pressure was 15.1±0.8 mm Hg in the dexmedetomidine group and 14.8±0.9 mm Hg in the neostigmine group, according to our research. The post-local intraocular pressure was similar in both groups.

Comparing dexamethasone and dexmedetomidine as an adjuvant to local anesthetic combination in peribulbar block, Alzeftawy and El Morad, (2018) found that IOP was lower in the dexmedetomidine group after injection compared to baseline reading (27).

Dexmedetomidine's potential to lower IOP is based on its ability to cause vasoconstriction of afferent blood vessels in the ciliary body, which in turn reduces aqueous humor output. It may also help with drainage of aqueous fluid by lowering the vasomotor tone of the eye's drainage system, which is controlled by the sympathetic nervous system (28).

Similar findings were reported by Awad et al. (2019) who found that reversing non-depolarizing neuromuscular blockade with neostigmine had no effect on intraocular pressure (IOP) (29).

In both groups of our study, patients' hemodynamics were within normal limits. Postoperative blood pressure, heart rate, and SO2 were not significantly different between neostigmine and dexmedetomidine groups.

Similarly, Alzeftawy and El Morad (2018) demonstrated in their research that patients' hemodynamics were unaffected by dexmedetomidine, with a steady hemodynamic profile across all measurement periods from preoperative to postoperative (27).

Also, Fayed *et al.*, (2018) revealed in their study that patients in dexmedetomidine groups were hemodynamically stable throughout the surgery (12).

In their research on neostigmine, Vasantha and Madhusudhana (2018) found that giving the drug intravenously reduced both heart rate and mean arterial blood pressure. Only one patient had bradycardia after receiving neostigmine dosages between 100 and 200 µg (30).

Similarly, the mean arterial blood pressure, heart rate, respiratory rate, and oxygen saturation were all steady during the surgical process and the study period in KS and Rajesh's (2019) comparison of the adjuvant impact of neostigmine and dexamethasone in caudal block for children (31).

5. Conclusions:

In conclusion, this research found that adding 50 µg of dexmedetomidine or 0.5 mg of neostigmine to the local anesthetic mixture in peribulbar anesthesia for cataract surgery shows that Dexmedetomidine was better than Neostigmine in faster onset of block, prolonged duration, low dose of local anesthetic needed.

Recommendations:

This study recommends that in peri-bulbar anesthesia, dexmedetomidine can be used as an adjuvant to a local anesthetic combination. In addition, the use of dexmedetomidine as an adjunct to local anesthesia warrants further investigation. Also, future research should focus on adjusting the dosage and studying the high-risk group and Dexmedetomidine's adjuvant effects in peripheral nerve blocks should be investigated further. Moreover, if dexmedetomidine is not available, neostigmine might be used instead.

6. References:

1. Friedman, D. S., Reeves, S. W., Bass, E. B., Lubomski, L. H., Fleisher, L. A., & Schein, O. D. (2004). Patient preferences for anaesthesia management during cataract surgery. British journal of ophthalmology, 88(3), 333-335.
2. Godarzi, M., Beyranvand, S., Arbabi, S., Sharoughi, M., Mohtaram, R., & Soltani, A. E. (2011). Comparing the effect of using atracourium and cis-atracourium as adjuvant agents to the local anesthetic substance on peribulbar-induced akinesia. Acta Medica Iranica, 509-512.
3. Loots, J. H., Koorts, A. S., & Venter, J. A. (1993). Peribulbar anesthesia: A prospective statistical analysis of the efficacy and predictability of bupivacaine and a lignocaine/bupivacaine mixture. Journal of Cataract & Refractive Surgery, 19(1), 72-76.

4. Soukup, O., Winder, M., Kumar Killi, U., Wsol, V., Jun, D., Kuca, K., & Tobin, G. (2017). Acetylcholinesterase inhibitors and drugs acting on muscarinic receptors-potential crosstalk of cholinergic mechanisms during pharmacological treatment. Current Neuropharmacology, 15(4), 637-653.
5. Eldufani, J., & Blaise, G. (2019). The role of acetylcholinesterase inhibitors such as neostigmine and rivastigmine on chronic pain and cognitive function in aging: A review of recent clinical applications. Alzheimer's & Dementia: Translational Research & Clinical Interventions, 5, 175-183.
6. Paris, A., & Tonner, P. H. (2005). Dexmedetomidine in anaesthesia. Current Opinion in Anesthesiology, 18(4), 412-418.
7. Gandhi, R., Shah, A., & Patel, I. (2012). Use of dexmedetomidine along with bupivacaine for brachial plexus block. National journal of medical research, 2(01), 67-69.
8. Bizrah, M., Ching, G., Yusuf, A. M., Din, N., Yeung, S. N., McCarthy, J. M., ... & Holland, S. P. (2022). Local anaesthesia as a standard of care for penetrating keratoplasty?. Eye, 36(7), 1486-1493.
9. Moolagani, V. R., Burla, S. R., Neethipudi, B. R., Upadhyayula, S. M., Bikkina, A., & Arepalli, N. R. (2019). Ropivacaine plus lidocaine versus bupivacaine plus lidocaine for peribulbar block in cataract surgery: A prospective, randomized, double-blind, single-center, comparative clinical study. Journal of Anaesthesiology, Clinical Pharmacology, 35(4), 498.
10. Sherif, N. A., Mohamad, M. K., Taher, S. G., Hannon, A. A., & Salem, H. M. (2019). Effectiveness and Safety of Single Percutaneous Peribulbar Block Using Magnesium Sulphate as an Adjuvant to Local Anesthetics the Standard Peribulbar Block for Strabismus Surgery in Adults. The Open Anesthesia Journal, 13(1).
11. Abd Elmoniem, M. F., & Kamel, R. M. (2019). Peribulbar block using dexmedetomdine versus magnesium sulphate as additives to local anesthetics for cataract surgery. The Egyptian Journal of Hospital Medicine, 75(4), 2679-2683.
12. Fayed, S. M., Mahdy, M. M., Ahmed, A. M., & Hefny, A. M. A. (2018). Comparative study between effects of addition of fentanyl versus dexmedetomidine to local anesthetic

mixture for peribulbar block for cataract surgery. The Egyptian Journal of Hospital Medicine, 72(8), 4984-4989.

13. Hafez, M., Fahim, M. R., Abdelhamid, M. H. E., Youssef, M. M. I., & Salem, A. S. (2016). The effect of adding dexmedetomidine to local anesthetic mixture for peribulbar block in vitreoretinal surgeries. Egyptian Journal of Anaesthesia, 32(4), 573-579.
14. Kassem, O.A., ELgarhy, A.M. and Salim, M.G., 2018. Magnesium sulphate versus Dexmedetomidine as adjuvants for local anasthetics in peribulbar block for eye surgeries: Clinical comparative study. The Egyptian Journal of Hospital Medicine, 72(4), pp.4308-4312.
15. Channabasappa, S. M., Shetty, V. R., Dharmappa, S. K., & Sarma, J. (2013). Efficacy and safety of dexmedetomidine as an additive to local anesthetics in peribulbar block for cataract surgery. Anesthesia, Essays and Researches, 7(1), 39.
16. Imani, F., Zaman, B., & De Negri, P. (2020). Postoperative pain management: Role of dexmedetomidine as an adjuvant. Anesthesiology and Pain Medicine, 10(6).
17. Ping, Y., Ye, Q., Wang, W., Ye, P., & You, Z. (2017). Dexmedetomidine as an adjuvant to local anesthetics in brachial plexus blocks: a meta-analysis of randomized controlled trials. Medicine, 96(4).
18. DNAP, L. S. F. (2016). Local anesthetic adjuvants providing the longest duration of analgesia for single-injection peripheral nerve blocks in orthopedic surgery: A literature review. AANA journal, 84(2), 95.
19. Aboul Fetouh, I. S., Sherif, N. A., Osama, N. A., & Mohamad, M. K. (2021). Safety and efficacy of adding different doses of neostigmine as an adjuvant in peribulbar block for cataract surgery: A randomized controlled trial. Egyptian Journal of Anaesthesia, 37(1), 349-355.
20. Edinoff, A. N., Fitz-Gerald, J. S., Holland, K. A. A., Reed, J. G., Murnane, S. E., Minter, S. G., ... & Kaye, A. D. (2021). Adjuvant drugs for peripheral nerve blocks: The role of NMDA antagonists, neostigmine, epinephrine, and sodium bicarbonate. Anesthesiology and Pain Medicine, 11(3).
21. Abd Elmoniem, M. F., & Kamel, R. M. (2019). Peribulbar block using dexmedetomdine versus magnesium sulphate as additives to local anesthetics for cataract surgery. The Egyptian

Journal of Hospital Medicine, 75(4), 2679-2683.

22. Prabhakar, A., Lambert, T., Kaye, R. J., Gaignard, S. M., Ragusa, J., Wheat, S., ... & Kaye, A. D. (2019). Adjuvants in clinical regional anesthesia practice: A comprehensive review. Best Practice & Research Clinical Anaesthesiology, 33(4), 415-423.
23. Muttu, S., Liu, E. H., Ang, S. B., Chew, P. T., Lee, T. L., & Ti, L. K. (2005). Comparison of dexmedetomidine and midazolam sedation for cataract surgery under topical anesthesia. Journal of Cataract & Refractive Surgery, 31(9), 1845-1846.
24. Kayalha, H., Mousavi, Z., Barikani, A. S., Yaghoobi, S., & Khezri, M. B. (2015). The effects of intrathecal neostigmine added to bupivacaine on postoperative analgesic requirement in patients undergoing lower limb orthopedic surgery. Middle East J Anaesthesiol, 23(2), 199-204.
25. Prasad, G. K., Khanna, S., & Jaishree, S. V. (2020). Review of adjuvants to local anesthetics in peripheral nerve blocks: Current and future trends. Saudi Journal of Anaesthesia, 14(1), 77.
26. Lauretti, G. R. (2015). The evolution of spinal/epidural neostigmine in clinical application: Thoughts after two decades. Saudi Journal of Anaesthesia, 9(1), 71.
27. Alzeftawy, A. E., & El Morad, M. B. (2018). Dexamethasone compared to dexmedetomidine as an adjuvant to local anesthetic mixture in peribulbar block for vitreoretinal surgery. A prospective randomized study. Anesthesia, Essays and Researches, 12(2), 359.
28. Bakr, R. H., & Abdelaziz, H. M. M. (2017). Rocuronium versus dexmedetomidine as an adjuvant to local anesthetics in peribulbar block: A double blind randomized placebo controlled study. Egyptian Journal of Anaesthesia, 33(3), 221-226.
29. Awad, A. A. E., Gharib, H. S., & El Said, T. M. (2019). Sugammadex versus neostigmine in reversal of rocuronium-induced neuromuscular block in obese patients. The Scientific Journal of Al-Azhar Medical Faculty, Girls, 3(1), 163.
30. Vasantha, N. S. K., & Madhusudhana, R. (2018). Intrathecal bupivacaine with neostigmine and bupivacaine with normal saline for postoperative analgesia: A cost-effective additive. Anesthesia, Essays and Researches, 12(2), 328.
31. KS, K., & Rajesh, K. V. (2019). Comparison of Postoperative Analgesia between Neostigmine and

Dexamethasone as an Adjuvant to Ropivacaine (0.25%) in Caudal Block Administered to Children under Sonographic Guidance.