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Effect of the use of dexmedetomidine as an adjuvant in peribulbar anesthesia in patients presented for vitreoretinal surgeries

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ABSTRACT

Background: Dexmedetomidine, if used in combination with a local anesthetic mixture in peribulbar anesthesia, may alter the block characteristic. This research aimed to study the influence of adding dexmedetomidine to local anesthetics in the peribulbar block.

Methods: Sixty adult patients of both gender presented for vitreoretinal surgeries were enrolled in this prospective double-blinded study. They were randomly distributed into two equal groups. All the patients received peribulbar anesthesia with 10 ml mixture composed of 4 ml of plain bupivacaine 0.5%, 4 ml of lidocaine 2 % containing 50 IU hyaluronidase, and either 2 ml of normal saline (Control group) or 20 μg dexmedetomidine in (Dexmedetomidine group). The onset, the duration, and quality of sensory and motor blockade and the perioperative sedation were recorded.

Results: As compared to the control group, dexmedetomidine when added to a local anesthetics in peribulbar block, significantly decreased the onset of anesthesia to 2.40 ± 1.50 min, fastened the onset of the lid akinesia to 2.93 ± 2.07 min and globe akinesia to 2.87 ± 1.96 min, increased the duration of lid akinesia to 137.00 ± 17.94 min and globe akinesia to 166.50 ± 21.34 min, and increased the time of the first request for postoperative analgesia to 185.83 ± 30.80 min ($P < .05$). Also, it significantly increased the level of patients sedation ($P < .05$).

Conclusion: A small dose of dexmedetomidine added to a local anesthetic mixture in peribulbar block improved the sensory and motor block criteria with increased level of patients sedation.

1. Introduction

Ophthalmic surgeries belong to the group of low risk surgeries owing to decreased risk of blood loss and/or fluid shift even with prolongation of the surgery [1]. However, patients undergoing retinal surgeries are often suffering from multiple co-morbidities as diabetes mellitus, hypertension, or cardiac disorders. These co-morbidities increase the anesthetic risk especially with the use of general anesthesia technique [2]. Therefore, local anesthetic techniques of the eye as peribulbar, retrobulbar, and sub-Tenons block are largely used for ophthalmic surgeries in many large centers all over the world [3,4]. It have advantage of decreased perioperative risk, improves postoperative analgesia, decreased cost, and improve the postoperative rehabilitation [5].

The peribulbar block is preferred over the retrobulbar block as it is easier, safer, and associated with a lesser complication [6]. In spite of that, its use may be limited or difficult owing to the longer surgery and the limited duration of the block [7]. Many agents, especially opioid analgesics, are used in combination with different local anesthetic mixture in order to improve the quality of regional block [8].

Dexmedetomidine, the highly potent and selective Alpha adrenergic 2 receptor agonist, was accepted by the United States Food and Drug Administration (FDA) to be used as sedative agents as it has sedative, sympatholytic, analgesic, and amnestic properties [9]. There are multiple studies evaluating the use of dexmedetomidine addition to different local anesthetics in epidural anesthesia [10], subarachnoid anesthesia [11,12], peripheral nerve block [13,14], and local anesthesia [15,16]. The use of dexmedetomidine as a local anesthetic adjuvant may alter the quality of the block. We aimed to study the effect of the addition of dexmedetomidine to local anesthetics in single injection peribulbar anesthesia for patients undergoing retinal surgeries. The primary outcome was the duration of globe akinesia, While, the onset and the duration of anesthesia were considered as secondary outcomes.

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2. Patients and methods

Up till now, dexmedetomidine wasn't accepted by the FDA for the perineural administration. Moreover, in our Country, there is no similar association for permission of new drugs usage. Thus, the perineural administration of dexmedetomidine was explained to the local ethical committee to detect that perineural administration of a dose of 20–100 μg is safe based upon previous similar studies [13,15,16], then, the study was approved by the ethical committee (Tanta Faculty of Medicine Research Ethics Committee 30690/01/2016). Then, the study had been registered on the Pan African Clinical Trial Registry since February 2016 with the unique identification number for the registry (PACTR201603001485381).

This controlled, randomized, double-blinded study was performed at the Ophthalmology Department of Tanta University Hospital. The study was started in February 2016, immediately after obtaining ethical committee approval, and lasted for one year. The study included adult patients aged 30–60 years old, of both sexes, with ASA physical status from I to III, scheduled for vitreoretinal surgeries.

All the patients were assessed preoperatively in the ophthalmic and anesthesia clinics, then, reassurance of the patients was done with an explanation of the purpose of the research. If the patient agreed to participate in the study, an informed written consent was obtained from him or herself. The patients were admitted to the operating room after 8 hours fasting from solid food and 2 hours fasting from clear fluids. All the data obtained in this research work were kept secret through secret codes and files and used only for this research work. Once the patients were admitted to the operating theater without premedication, they were reassured with obtaining intravascular venous access through peripherally inserted 20 gauge venous cannula, then, the patients were attached to the monitor in the form oxygen saturation, 5 leads electrocardiogram, and non-invasive blood pressure. A nasal cannula was used at a flow rate of 2–4 l/min to supply oxygen to patients. An anesthesiologist resident who was blinded to the study was used to prepare the local anesthetic mixture in uniform syringes and introduce them in a sealed envelopes.

Exclusion criteria were consisted of, refusal of patients to participate, unconscious or uncooperative patients, the coexistence of glaucoma or ocular infection, suspected or diagnosed coagulopathy, or patients with uncontrolled cardiac conditions. The patients were randomly allocated into two equal groups through computer generated randomization in sealed opaque envelops to allow every patient to choose his own group (Fig. 1).

Control group (C group) (30 patients); Patients in this group received peribulbar block with 10 ml of a local anesthetic mixture composed of 4 ml of plain bupivacaine 0.5%, 4 ml of lidocaine 2% containing 50 IU hyaluronidase, and 2 ml of normal saline.

Dexmedetomidine group (D group) (30 patients); The local anesthetic mixture received in patients of this group was composed of 4 ml of plain bupivacaine 0.5%, 4 ml of lidocaine 2% containing 50 IU hyaluronidase, and 20 μg of dexmedetomidine dissolved in 2 ml (Total volume 10 ml).

Disposable needles in a size of 25 gauge and 16 mm bevels were used to perform the peribulbar injection. The injection site was limited by the lateral nasal margin laterally, inferior orbital margin inferiorly, and the lower lacrimal punctum superiorly [17]. Once the needle was introduced, the patient was asked to look in the four cardinal directions of the gaze, superior, inferior, nasal, and temporal to ensure that the needle wasn't penetrating the eye globe, then negative aspiration was done to exclude intravascular position of the needle, then, the peribulbar injection of previously prepared local anesthetic mixture was performed over 30 seconds and followed by fullness of the eye lids. The eye lids were closed and covered by eye pads carefully with an application of 20 mmHg pressure through an intermittent application of Honan ball for 10 min. The intermittent eye compression was relieved after 1 min, 3 min, 5 min, 7 min, 9 min, and 10 min to assess the onset and the quality of sensory and motor blockade. All the intraoperative or postoperative measurements were obtained by the aid of an assistant nurse who wasn't participating in the study.

Sensory block was assessed by the abolishment of corneal reflex to instillation of physiological drops on the cornea or conjunctiva. The onset of anesthesia was determined by the time interval from local anesthetics injection and loss of corneal reflex. The motor block was evaluated by asking the patient to open, close, and squeeze his eye (Lid Akinesia) and to move his eye globe in the four directions of the gaze (globe akinesia). The quality of akinesia was assessed through the use of akinesia score where 0 = inability to move (total akinesia), 1 = partial movement (partial akinesia), and 2 = full movements (no akinesia). This score was used to assess both lid akinesia and globe akinesia in the four directions with the overall score of 10 [18]. The onset of lid akinesia was calculated from peribulbar injection to the partial loss of ability to open or squeeze eye lids, while, the onset of globe akinesia was estimated from the injection of the local anesthetic mixture and partial loss of movement of eye globe in the four cardinal directions. The surgery was considered to be optimal to be started when the patient had corneal anesthesia together with partial lid and globe akinesia. The optimal time to start the surgery was considered as the elapsed time between local anesthetics injection and satisfying the goals to start the surgery. The intraocular pressure was measured preoperatively and immediately before initiating the surgery with detection of number of patients with increase in the intraocular tension (increase intraocular pressure more than 25 mmHg or by more than 10 mmHg than the preoperative value)

The duration of sensory block was estimated to be the time interval from the peribulbar injection till regaining corneal sensation, while, the duration of lid or globe akinesia was determined by the time elapsed between performing the peribulbar injection and the full regaining of lid or globe movement respectively. The Ramsay Sedation Score (Table 1) [19] was used to evaluate the patients level of sedation in the intra and postoperative periods as it was measured every 15 min from the start of the surgery and measured every 2 h after completing the surgery till 12 h. In the postoperative period, the visual analogue score (VAS) which is composed of 0–10 score was used to assess the severity of postoperative pain (where 0 = no pain and 10 = severe pain), The VAS score was evaluated 1 h, 2 h postoperative, then every 2 h till 12 h. Any patients with VAS score more than 4 received rescue analgesia in the form of 50 mg tramadol intravenous injection together with 500 mg paracetamol by intravenous infusion with calculation of the time for the first call of postoperative analgesia. Any detected complication as nausea and vomiting, pain on injection, or increased intraocular tension was recorded.

3. Statistical analysis

Based on the results of the previous study [16] calculation of sample size revealed that, at least twenty-six patients were required in each group to detect a significant difference of 45 minutes in the duration of the motor blockade at alpha error 0.05 and power of study 90%. The statistical analysis was carried out by the use of (SPSS Inc., Chicago, IL, USA). Categorical data, except ASA class, were analyzed by Fisher's exact test and expressed as number and percent. While ASA class was analyzed by the aid of Chi-Squared test and presented as number and percentage. Parametric data were expressed as a mean and standard deviation after analysis through the unpaired T test. Statistically significant changes were considered when the p value was less than 0.05.

4. Results

Seventy-three patients were assessed for eligibility to participate in this study, five of them refused to participate, while eight of them were not meeting our inclusion criteria, so, thirteen patients were excluded from the study while the remainder sixty patients were randomly

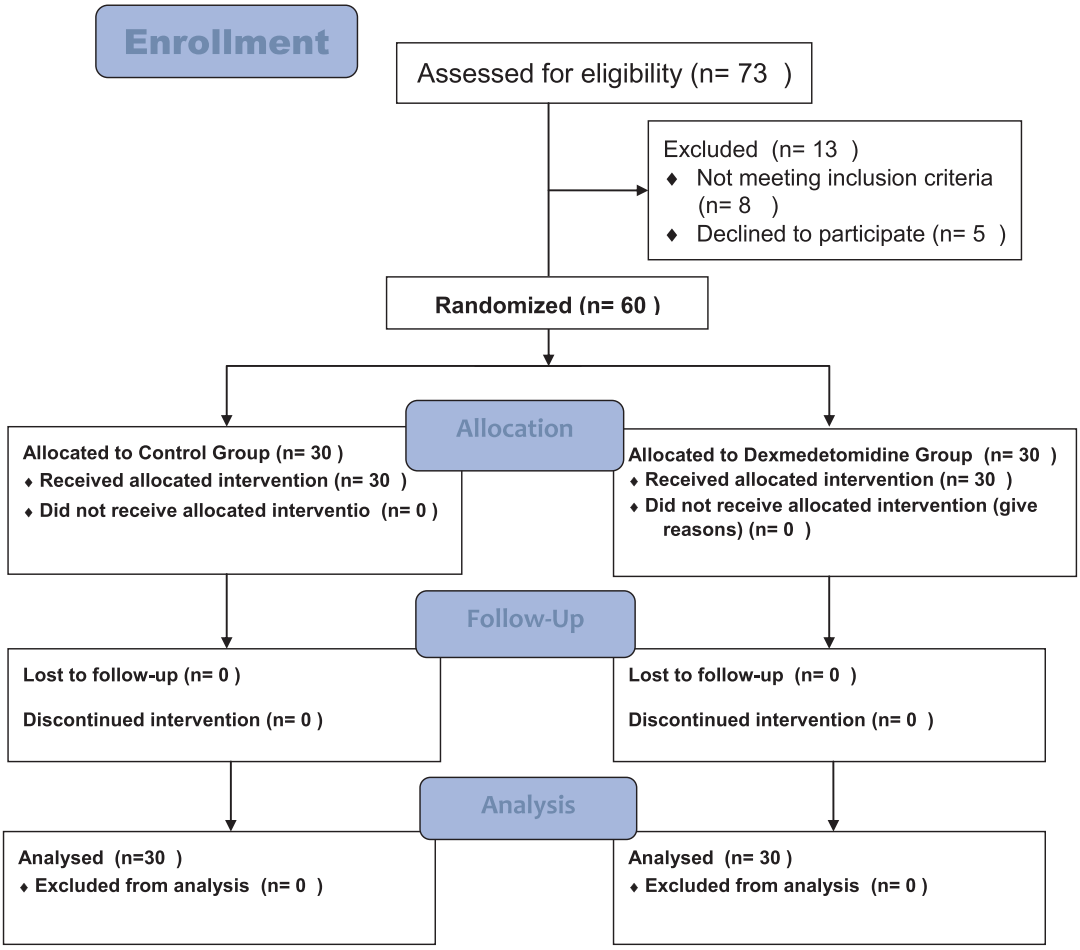

Fig. 1. Flow chart of distribution of patients through each step of the research.

Table 1
The Ramsay sedation score.

Score	Observations
1	Anxious, agitated, or restless
2	Cooperative, oriented, and tranquil
3	Responds to commands
4	Asleep, but with brisk response to light glabellar tap or loud auditory stimulus
5	Asleep, sluggish response to glabellar tap or auditory stimulus
6	Asleep, no response

allocated into two equal groups (Fig. 1). The results of both patients and surgical characteristics, including age, gender, body weight, ASA class, the axial length of the globe, side, or duration of surgery were comparable between both groups (P > .05). No major or serious complications occurred in either of the two studied groups, the incidence of nausea and vomiting, increased intraocular tension, or pain on peribulbar injection was insignificant statistically between the two studied groups (P > .05) (Table 2).

The onset of corneal anesthesia was significantly faster in dexmedetomidine group as compared to the control group (P = .006). Moreover, the onset of both lid and globe akinesia were significantly decreased with the use of dexmedetomidine as compared to the control group (P = .046, .002). The results of dexmedetomidine group revealed significant prolongation of the duration of lid or globe akinesia in comparison to the control group (P = .0003, .003). Also, the time required to start the surgery was much more decreased in the dexmedetomidine group than the control group (P = .008). Added to that, the time of the first request of analgesics was prolonged significantly in the dexmedetomidine group compared to the control group (P = .004) (Table 3).

The results of the quality of the motor blockade assessed by akinesia score, including both lid and globe, were comparable at 1 min, 3 min, and 5 min after the peribulbar injection (P = .33, .06, and .09 respectively). However there was significant decrease in the akinesia score in the dexmedetomidine group as compared to the control group at 7 min, 9 min, and 10 min after the peribulbar injection (P = .047, .038, and .047 respectively) (Fig. 2).

The mean values of postoperative Visual Analogue Scale were statistically insignificant between the two studied groups, immediately postoperative, 2 h, 4 h, 6 h, 8 h, 10 h, and 12 h after the surgery (P > .05) However, one hour after the surgery, the values of VAS in the dexmedetomidine group were significantly lower than that of the control group (P = .02) (Fig. 3).

During the intraoperative period, the level of patients sedation assessed by the Ramsay Sedation Score, revealed statistically significant increase in the level of sedation in the dexmedetomidine group than in the control group within 30 minutes, 45 min, 60 min, and 75 min from the peribulbar injection (P < .05) while, after 15 min from the injection, the Ramsay Sedation Score values were comparable among the two studied groups (P = .58). During the postoperative period, the patients of the dexmedetomidine group showed a significantly higher level of sedation than the patients of the control group at 2 h, 4 h, and 6 h postoperatively (P = .005, .001, and .007 respectively). However, the level of patients sedation was insignificant among the two studied groups at 8 h, 10 h, and 12 h of the postoperative period (P > .05) (Fig. 4).

Table 2
Patients and surgical characteristics.

		Control group	Dexmedetomidine group	P-Value	CI (95%)
Age (years)		47.73 ± 8.89	47.80 ± 9.01	0.977	−4.559; 4.693
Gender	Male	15 (50.00%)	17 (56.67%)	0. 796	0.5280; 1.450
	Female	15 (50.00%)	13 (43.33%)		
Body Weight (kg)		89.00 ± 6.70	86.70 ± 7.59	0.219	−6.001; 1.401
ASA Class	Class I	13 (43.33%)	13(43.33%)	0.935	
	Class II	12 (40.00%)	11 (36.67%)		
	Class III	5 (16.67%)	6 (30.00%)		
Axial length (mm)		27.53 ± 3.67	27.43 ± 3.73	0.917	−2.011; 1.811
Duration of surgery (min)		52.47 ± 5.94	52.77 ± 5.32	0.837	−2.613; 3.213
Site of surgery	Right	14 (46.67%)	16 (53.33%)	0. 797	0.284; 1.835
	Left	16 (53.33%)	14 (46.67%)		
Complications	Increased intraocular tension	3 (10%)	5 (16.67%)	0.707	0.284; 1.835
	Pain on injection	5 (16.67%)	7 (23.33%)	0.748	0.388; 1.648
	Nausea & Vomiting	4 (13.33%)	7 (23.33%)	0.506	0.300; 1.564

CI; Confidence interval.
Data presented as mean and standard deviation or as a number and percentage.

Table 3
Characteristic features of the peribulbar block in the studied groups.

	Control group	Dexmedetomidine group	P	CI (95%)
Onset of Anesthesia (min)	3.87 ± 2.39	2.40 ± 1.50	0.006*	0.436; 2.497
Onset of lid akinesia (min)	4.20 ± 2.71	2.93 ± 2.07	0.046*	0.022; 2.512
Onset of globe akinesia (min)	4.87 ± 2.73	2.87 ± 1.96	0.002*	0.773; 3.227
Duration of lid akinesia (min)	121.50 ± 12.67	137.00 ± 17.94	0.0003*	7.474; 23.526
Duration of globe akinesia (min)	152.00 ± 14.06	166.50 ± 21.34	0.003*	5.161; 23.839
Time required to start surgery (min)	5.53 ± 2.10	4.00 ± 2.21	0.008*	0.419; 2.647
Time for the first request for analgesia (min)	165.33 ± 21.21	185.83 ± 30.80	0.004*	6.834; 34.166

Data were presented as mean ± SD. P represented comparison between three groups.
* Denotes significant change. CI; Confidence interval.

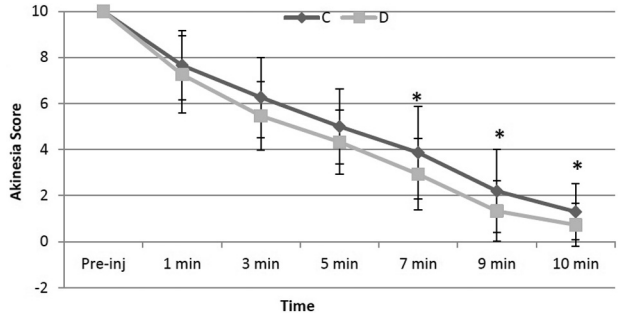

Fig. 2. Lid and globe akinesia score in the studied patients. Data were expressed as mean values ± standard deviation. * denotes significant difference among two groups.

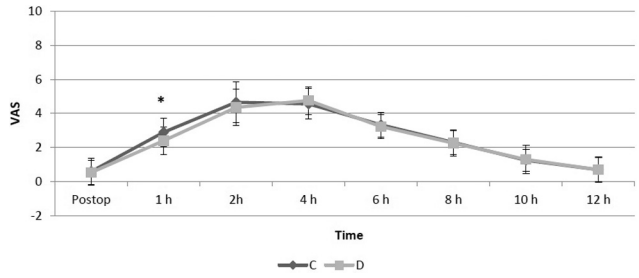

Fig. 3. Visual analogue score in the two groups. Data were expressed as mean values ± standard deviation. * denotes significant change between the two groups.

5. Discussion

The results of this study revealed that the use of dexmedetomidine as an adjuvant to local anesthetic mixture in patients undergoing vitreoretinal surgeries under single injection percutanous peribulbar anesthesia was associated with shortening of the onset of sensory and motor block, prolongation of the duration of lid and globe akinesia and the duration of postoperative analgesia, improvement of the quality of lid and globe akinesia, and increased the level of patients sedation. Despite that, the use of dexmedetomidine wasn't associated with significant change in the postoperative Visual Analogue Score.

The mechanism of analgesic and sedative effect with the use of dexmedetomidine isn't fully understood. Alpha 2 adrenoreceptors agonists may exert its analgesic effect through hyperpolarization of the non-adrenergic neurons which leads to depression of neuronal firing in the locus ceruleous together with suppression of the release of norepinephrine as a result of the stimulation of the central adrenergic receptors which produces a hypnotic effect without ventilatory depression [20]. Also, stimulation of α2-Adrenergic receptor in the superficial dorsal horn neurons produces an antinociceptive effect through suppression of the release of certain chemical mediators as glutamate from the afferent terminals. The bradycardia that may occur with the use of dexmedetomidine is usually due to activation of the post-synaptic α2 receptors [21].

Although there is a lack of available studies evaluating the use of dexmedetomidine as an adjuvant to local anesthetics in peripheral nerve block, certain studies were in concordance with our results. Ghali et al. [16], concluded that the addition of 20 μg of dexmedetomidine to levobupivacaine in Sub-Tenon's anesthesia for patients presented for vitreoretinal surgeries improved the characteristics features of the sensory and the motor block with a significant increase in the level of patients sedation. Also, Wu et al. [22], in a meta-analysis that included 16 randomized controlled trials and involved 1092 patients revealed that, adding dexmedetomidine to a local anesthetic agents in neuraxial anesthesia was associated with a significant improvement in the onset, the duration, and the quality of analgesic effect with significant sedation of the patients without significant increase in the incidence of side effect or complication except the bradycardia. Moreover, Abdallah and

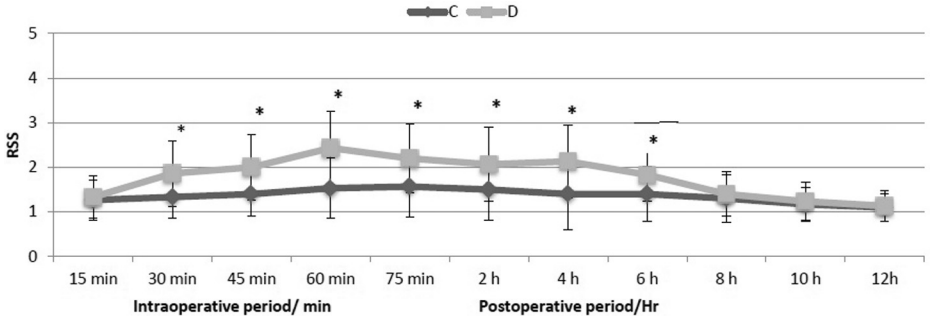

Fig. 4. Ramsay sedation score of the patients of the two studied groups. Data were expressed as mean values ± standard deviation. * denotes significant difference between the two groups.

Brull [23], in their systematic review and meta-analysis found that, dexmedetomidine, when added to the local anesthetics as adjuvant improved the sensory and the motor criteria of the block with significant improvement of the postoperative analgesia. Perineural administration of dexmedetomidine showed moderate to deep sedation of the patients without severe side effects or complications.

In addition, Dutt et al. [24] studied the effect of addition of either fentanyl or dexmedetomidine to ropivacaine in caudal block in children presented for lower abdominal surgeries and demonstrated that the use of dexmedetomidine was associated with more prolonged analgesic effect than fentanyl with mild degree of arousable sedation and insignificant changes in hemodynamic parameters. Also, Selim et al. [25], in their study that evaluated the addition of either fentanyl or dexmedetomidine to plain bupivacaine in epidural labour analgesia concluded that the use of dexmedetomidine as adjuvant to the local anesthetics in epidural labour analgesia was associated with better onset, duration, and quality of analgesia as compared to the use of fentanyl.

Moreover, Kamal and Talaat [26], compared the use of epidural morphine and epidural dexmedetomidine as an adjuvant to levobupivacaine in major abdominal surgery and revealed dexmedetomidine can be used as a good alternative to morphine as a local anesthetic adjuvant as it was associated with comparable analgesic effects. Moreover, Bajwa et al. [27], compared the use of either dexmedetomidine or fentanyl as an adjuvant to ropivacaine in epidural anesthesia for lower limbs surgeries and concluded that dexmedetomidine represents a good alternative to fentanyl as a local anesthetic adjuvant as its use was associated with better analgesic characteristics.

In addition, Obayah et al. [28], evaluated the effect of the addition of dexmedetomidine to the local anesthetics in bilateral greater palatine nerve block in children presented for cleft palate repair under general anesthesia and revealed that dexmedetomidine prolonged the duration of greater palatine nerve block. Also, Fyneface-Ogan et al. [29], who evaluated the addition of either fentanyl or dexmedetomidine as an additive in single shot spinal anesthesia for labour analgesia and demonstrated that the use of dexmedetomidine was associated with a better analgesic properties as compared to the use of fentanyl.

In contrast to the results of our study, Esmaoglu et al. [30], who revealed that addition of dexmedetomidine to lidocaine in intravenous regional anesthesia wasn't associated with any effect on the duration of either sensory or motor blockade. Also, Gandhi et al. [31], concluded that the use of dexmedetomidine as a local anesthetic adjuvant in supraclavicular brachial plexus block delayed the onset of sensory and motor block. However, they were in agree with our findings that the use of dexmedetomidine decreased the postoperative pain and the need for analgesics.

5.1. Limitation of the study

This study was limited by the small number of participating patients. Moreover, there is hardly a small number of available studies for assessment of the safety and efficacy of the use of dexmedetomidine as an additive in peribulbar, retrobulbar, or sub-Tenons block.

6. Conclusion

In a conclusion, adding a small dose of dexmedetomidine (20 μg), the α2-Adrenergic receptor agonist, to a local anesthetic mixture composed of lidocaine containing hyaluronidase and plain bupivacaine in the single injection percutaneous peribulbar block significantly decreased the onset of anesthesia and akinesia, prolong the duration of sensory and motor block, and decreased postoperative analgesic consumption. Also, dexmedetomidine led to moderate sedation of the patients throughout the perioperative period. No major complications or side effects had occurred with the use of dexmedetomidine.

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Conflict of interest

No conflict of interest.

Author contribution

Sameh Abdelkhalik Ahmed contributed in formulation of the study design, analysis and interpretation of the data, and final revision and submission.

Mohamad Gamal Elmawy made a contribution in the collection of the data, drafting, and revising the article. Also, he gave final approval to the final format of the article.

Amr Ahmed Magdy participated in collection and analysis of the data and final revision of the article.

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