Original Article

Evaluation of the effect and safety of dexmedetomidine as an additive to local anesthesia in peribulbar block for vitreoretinal surgery

Gaganjeet S Gujral, Manisha Agarwal, Preety Gautam[1], Ankita Shrivastav, Shalini Singh

Purpose: We conducted a prospective, randomized study to evaluate the efficacy of dexmedetomidine as an additive to peribulbar block for vitreoretinal surgery in terms of onset time of block, hemodynamic stability profile, patient comfort, and surgeon satisfaction. **Methods:** One hundred patients of American Society of Anesthesiologists grade 1 and 2 scheduled for vitreoretinal surgery were randomly assigned into two groups: control group (n = 50) received lignocaine bupivacaine block, and Dex group (n = 50) received lignocaine bupivacaine plus 20 μg dexmedetomidine peribulbar block. Information regarding time for onset of block, hemodynamic data, visual analog scale for pain, sedation levels, total duration of surgery, and surgeon satisfaction levels were collected. **Results:** All the demographic characteristics including age, gender, American Society of Anesthesiologists grade, onset of anesthesia, and duration of surgery were comparable in both groups. At the baseline, there was no statistically significant difference in heart rate, mean arterial pressure, diastolic blood pressure, and respiratory rate between the two groups, with a difference noted in systolic blood pressure at the baseline. There was significant difference noted in the systolic blood pressure and mean arterial pressure at different time intervals with a decreasing trend as time progressed. The mean sedation score was significantly higher in the Dex group than that in the control group. The surgeon satisfaction was higher in the Dex group than that in the control group. **Conclusion:** Dexmedetomidine is a useful and safe drug in combination with lignocaine bupivacaine in peribulbar for vitreoretinal surgery as it maintains hemodynamic stability and provides sedation, which enables full cooperation and potentially better operating conditions.

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1386_18

Quick Response Code:

Key words: Dexmedetomidine, patient comfort, peribulbar block, surgeon satisfaction, vitreoretinal surgery

Ocular surgeries are performed under topical, regional, or general anesthesia. The most common being peribulbar blocks/anesthesia, which often has a delayed onset of anesthesia and akinesia, short duration of analgesia, and a frequent need for block supplementation. Many additives such as hyaluronidase are being used to overcome these drawbacks.[1,2]

Dexmedetomidine (DEX) is a potent α2 adrenoceptor agonist.[3] It provides dose-dependent sedation, analgesia, sympatholysis, and anxiolysis without significant respiratory depression, and it for these properties that DEX has been used as an additive in peripheral nerve block, brachial plexus block, and in intravenous regional anesthesia.[3-6]

Vitreoretinal surgeries are of longer duration in comparison to cataract surgeries. Intraoperative hemodynamic stability plays an important role in vitreoretinal surgeries which have a risk of intraoperative bleeding, specially during diabetic vitrectomies and vision threatening expulsive choroidal hemorrhage. Hence, we evaluated the properties of DEX as an additive to peribulbar block for vitreoretinal surgeries, which might prove to be beneficial to the patient in terms of safety and comfort and act as an important tool in the armamentarium of the vitreoretinal surgeon.

Methods

A prospective, randomized, case control study was performed at a tertiary eye care center of North India over a period of 9 months. The study was approved by the Institutional ethics committee and conformed to the Declaration of Helsinki. Patient informed written consent was obtained before patient enrolment. Randomization was done using computer-generated random permuted blocks to equalize the number of patients undergoing each treatment. Assuming a standard deviation of 15 units of change for each group, the study required a sample size of 48 for each group (i.e., a total sample size of 96, assuming equal group sizes) to achieve a power of 90% and a level of significance of 5% (two-sided), for detecting a true difference in means between the two group of 10 units. A total of 100 patients were included in this study.

The inclusion criteria were as follows:

- Age: 18–70 years of either gender
- American Society of Anesthesiologists (ASA) physical status I and II.

Departments of Vitreoretina and [1]Anesthesia, Dr. Shroff's Charity Eye Hospital, New Delhi, India

Correspondence to: Dr. Manisha Agarwal, Department of Vitreoretina, Dr. Shroff's Charity Eye Hospital, Daryaganj, New Delhi - 110 002, India. E-mail: manisha@sceh.net

Manuscript received: 18.09.18; Revision accepted: 03.01.19

Cite this article as: Gujral GS, Agarwal M, Gautam P, Shrivastav A, Singh S. Evaluation of the effect and safety of dexmedetomidine as an additive to local anesthesia in peribulbar block for vitreoretinal surgery. Indian J Ophthalmol 2019;67:636-40.

The exclusion criteria was as follows:

- Hypersensitivity to study drug
- Significant cardiovascular disease (second [Mobitz II type] or third degree heart block)
- Congestive heart failure
- Chronic heart failure (New York heart association [NYHA] III-IV)
- Body mass index (BMI) >35
- Uncontrolled diabetes
- Renal/hepatic impairment
- Chronic obstructive pulmonary disease
- Chronic clonidine therapy
- Alcohol abuse/coagulopathy/pregnancy
- Patients on antipsychotics and antiepileptics.

The essence of this study was to evaluate the systemic effects of adding DEX to the peribulbar block. Hence, the primary outcome measures included the hemodynamic profile of patients during surgery. Secondary outcome measures included time of pain and sedation scales of patient, onset of block and block supplementation (if required), surgeon satisfaction score, and adverse effects (if noted) due to the anesthesia.

In the control group – 6 ml of (0.5% bupivacaine admixed with 450 IU of hyaluronidase) +3 ml of 2% lignocaine + 1 ml of normal saline was used for peribulbar block; and in the Dex group – 6 ml of (0.5% bupivacaine admixed with 450 IU of hyaluronidase) +3 ml of 2% lignocaine + 1 ml of DEX (20 μg) was used.

All patients were operated by a single surgeon. The peribulbar block was given by the same surgeon. The surgeon and the assistant monitoring the parameters during the surgery were masked to the contents of the block.

Preanesthetic evaluation and fasting status of 4 h was ensured. Premedication such as sedative drugs was not allowed.

Preoperatively, baseline vital parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), and peripheral oxygen saturation (SpO_2) were noted.

In all patients, complete 10 ml of peribulbar block mixture was used. A total of 6 ml of the anesthetic mixture was given inferiorly with a 23-gauge needle at the junction of outer one-third and inner two-third of the lower orbital rim above the superior orbital notch. The remaining 4 ml was given superonasally beneath the superior orbital notch. Block supplementation, if given, was noted. The amount used for supplementation was 4 ml of the control group block in all cases that required supplementation. Block supplementation was given in the inferior fornix below the lateral limbus.

After the peribulbar block was given, ocular movements were evaluated at 15 s interval in all four directions using three-point scale – 0: complete akinesia, 1: limited movements, and 2: normal movements. Onset of block was calculated from the time of injecting of local anesthesia till the ocular movements were of grade ≤1.

Visual analog scale (VAS) for pain (on a scale from 0 to 10) was recorded at the baseline (T0), 2 min (T1), and 5 min (T2) after peribulbar block and at the end of the surgery (Te).[7]

Intraoperative monitoring included electrocardiogram, blood pressure, pulse oximetry, and respiratory rate every 10 min during surgery. Sedation levels were assessed with modified Ramsay sedation scale at every 10 min during surgery using the following grades: Grade 1 = Anxious and agitated or restless or both; Grade 2 = cooperative, oriented, and tranquil; Grade 3 = responds to commands only; Grade 4 = brisk response to light glabellar tap or loud auditory stimulus; and Grade 5 = no response to light glabellar tap or loud auditory stimulus.[8]

Adverse effects, if any (bradycardia (heart rate <20% of baseline), hypotension (MAP <20% of baseline), respiratory rate depression (RR <10/min), and oxygen desaturation (SpO_2 <92%) were noted and treated.

Surgeon satisfaction was evaluated at the end of the surgery using a five-point Likert scale – Completely satisfied: patients with painless, quiet, and ideal surgical conditions; Satisfied: patients with some painful expression, slight anxiety, and good surgical conditions; Slightly dissatisfied: patients with moderate pain, anxiety, and adequate surgical conditions; Dissatisfied: patients with severe pain, anxiety, and suboptimal surgical conditions; and Very dissatisfied: patients with severe pain, restlessness, and inadequate surgical conditions.

Statistical Package for the Social Sciences software version 23 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Mean and standard deviation was calculated for continuous variables. Categorical variables were reported in percentages. The one-way analysis of variance (ANOVA) was used to determine the differences between the means of hemodynamic parameters at different time points. Bonferroni method was used for performing post hoc analysis. For continuous variables, independent *t*-test was used to determine the difference between the two groups. Chi-square test was used to compare categorical variables between the two groups. A probability (*P*) of 0.05 or less was considered statistically significant.

Results

A total of 100 patients (50 in each group) were enrolled in the study. Seventy-two of them were males and 28 were females. Gender ($P = 0.37$), age ($P = 0.09$), ASA grade ($P = 0.23$), and time to onset of anesthesia ($P = 0.1$) were comparable between the two groups [Table 1]. The mean duration of surgery in Dex group was 76.3 ± 24.6 min and in control group was 70.3 ± 25.4 min ($P = 0.23$). The distribution of duration of surgeries in different quartiles has been shown in Fig. 1. In the Dex group, preoperative diagnosis was as follows: 28 patients were of rhegmatogenous retinal detachment (RRD), 12 patients were of tractional retinal detachment (TRD) due to diabetic retinopathy (DR), and 10 patients were of vitreous hemorrhage (VH) due to vascular occlusive disease/vasculitis. In the control group, preoperative diagnosis was as follows: 33 patients were of RRD, 11 patients were of TRD due to DR, and 6 patients were of VH.

Eight patients required supplementation of block in the control group and 3 patients required supplementation in the Dex group. This was not statistically significant ($P = 0.110$).

The VAS scoring for pain was comparable in both the groups at 2 min interval. In the control group, at 5 min interval, 1 patient was in grade 1, 33 patients were in grade 2, 15 patients were in grade 3, while 1 patient was in grade 4; at completion, 30 patients were in grade 2, 18 patients were in grade 3, while 2 patients were in grade 4. In the Dex group, at 5 min interval, 47 patients were in grade 2 while 3 patients were in grade 3; at completion, 45 patients were in grade 2 while 5 patients were in grade 3. It was found to be lower at 5 min interval ($P = 0.006$) and at completion of the surgery ($P = 0.007$) in the Dex group.

At baseline (0 min), no statistically significant difference was noted in HR ($P = 0.06$), MAP ($P = 0.38$), DBP ($P = 0.68$), and RR ($P = 0.07$) between the two groups. However, the mean SBP value differed significantly between the two groups ($P = 0.04$), with the mean SBP reading in the control group being 138.92 mmHg and in the Dex group being 132.80 mmHg at the baseline.

One-way ANOVA analysis revealed that in Dex group the mean HR ($P = 1.0$), DBP ($P = 0.71$) [Fig. 2], and RR ($P = 0.36$) did not change significantly at different time points. Similarly in the control group, mean HR ($P = 0.38$), MAP ($P = 0.47$), DBP ($P = 0.67$), SBP ($P = 0.8$), and RR ($P = 0.91$) did not change significantly at different time points.

Table 1: Demographic profile and characteristics of all the patients

Patient characteristics	Control group (*n*=50)	Dex group (*n*=50)	*P*
Age (years) (mean±SD)	49.72±15.3	44.64±14.4	0.092
Gender (Male:Female)	34:16	38:12	0.373
ASA* grade 1	22	28	0.230
ASA grade 2	28	22	
Block onset time (seconds) (mean±SD)	121.48±50.2	104.94±50.6	0.104
Surgery Duration (Minutes) (mean±SD)	70.34±25.4	76.36±24.6	0.238

*American society of anesthesiologists

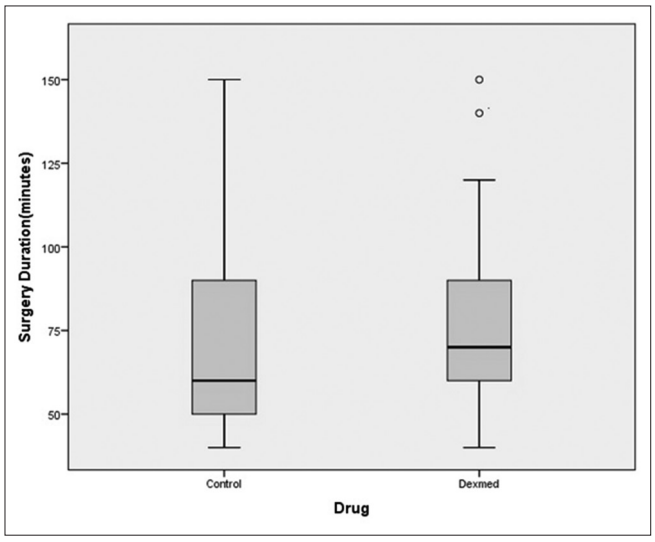

Figure 1: Box plot representing the surgery duration in the control and Dex group

The mean MAP in Dex group was statistically significant at different time points (one-way ANOVA, $P = 0.03$). Post hoc analysis revealed that mean MAP value did not change from 0 min to 10 min ($P = 1.0$), 20 min ($P = 1.0$), and 30 min ($P = 0.71$). There was significant decrease from 0 min to 40 min ($P = 0.04$) and 50 min ($P = 0.032$). After this, the change was not statistically significant, i.e., from 0 min to 60 min ($P = 0.13$), 70 min ($P = 0.63$), 80 min ($P = 1.0$), and 90 min (1.0) [Fig. 3].

The mean SBP in Dex group was statistically significant at different time points (one-way ANOVA, $P = 0.01$). *Post hoc* analysis revealed that the mean SBP value did not change significantly from 0 min to 10 min ($P = 1.0$), 20 min ($P = 1.0$), 30 min ($P = 0.71$), 40 min ($P = 0.13$), 50 min ($P = 0.07$), 60 min ($P = 0.1$), 70 min ($P = 0.61$), 80 min ($P = 1.0$), and 90 min (1.0) [Fig. 4]

The mean sedation score in Dex group was statistically significant at different time points (One-way ANOVA, $P = 0.01$). The mean of sedation score readings at 10^{th}, 20^{th}, 30^{th}, 40^{th}, 50^{th}, 60, 70^{th}, 80^{th}, and 90^{th} min for Dex group was 2.56, 2.74, 2.90, 3.02, 2.98, 2.92, 2.95, 2.98, and 3.04, respectively, and for control group was 2.14, 2.30, 2.56, 2.52, 2.51, 2.45, 2.32, and 2.36, respectively. *Post hoc* analysis revealed that the mean sedation score value in the Dex group had changed significantly from 0 min to 10 min ($P = 0.00$), 20 min ($P = 0.00$), 30 min ($P = 0.00$), 40 min ($P = 0.00$), 50 min ($P = 0.00$), 60 min ($P = 0.00$), 70 min ($P = 0.00$), 80 min ($P = 0.00$), and 90 min (0.00). However, the change was not significant between 10 min and 20 min ($P = 1.0$), 20 min and 30 min ($P = 1.0$), 30 min and 40 min ($P = 1.0$), and so on up to 90 min. The mean sedation score was significantly higher in the Dex group than the control group ($P < 0.05$) at all readings.

The surgeon satisfaction at the end of the surgery was higher in the Dex group than that in the control group ($P = 0.05$). In the Dex group, the surgeon was completely satisfied in 35 cases and slightly dissatisfied in 1 case. In the control group, the surgeon was completely satisfied in 27 cases and slightly dissatisfied in 7 cases.

There were no adverse effects noted due to the anesthesia in both the control and Dex group.

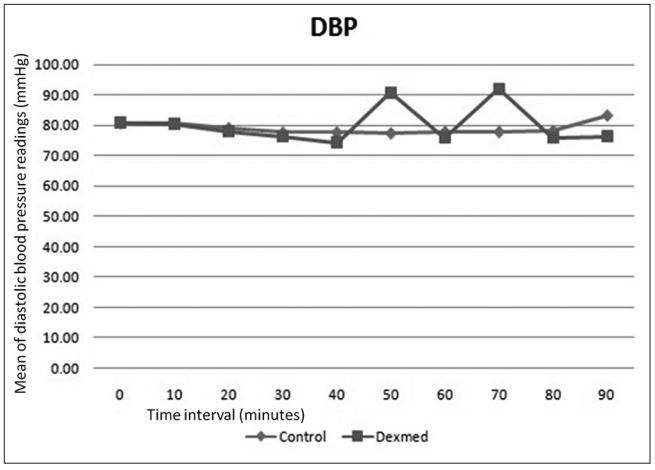

Figure 2: Graphical representation of diastolic blood pressure changes at different time intervals in both control and Dex group

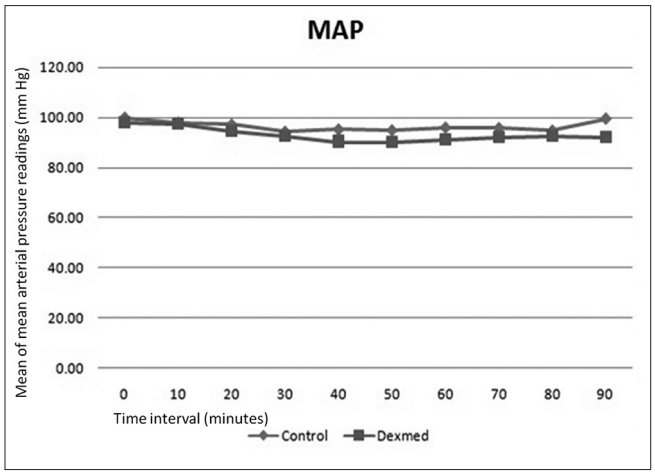

Figure 3: Graphical representation of mean arterial pressure changes at different time intervals in both control and Dex group

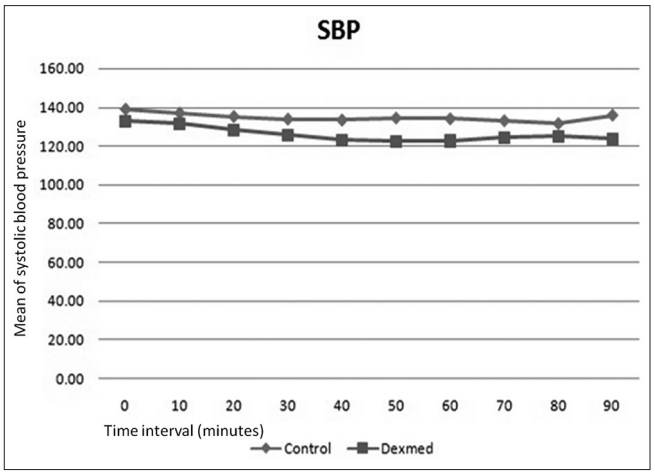

Figure 4: Graphical representation of systolic blood pressure changes at different time intervals in both control and Dex group

Discussion

The most commonly performed surgery in ophthalmology is a cataract surgery. The average duration of a cataract surgery is short varying between 15 and 30 min. The commonly used method of anesthetizing the eye is by a peribulbar block which is said to provide the same anesthetic effect as a retrobulbar injection but with a lower rate of complications.[9] Vitreoretinal surgeries are more complex, of a longer duration, and the patients are often suffering from various systemic diseases such as diabetes, coronary artery disease, and hypertension requiring constant monitoring of systemic parameters during the course of the surgery.

Many additives such as clonidine, hyaluronidase, sodium bicarbonate, muscle relaxants, and opioids are added to local anesthetic drugs in the peribulbar block for a rapid onset of action and longer duration of the analgesic effect.[1,2]

Alpha 2 adrenergic receptor agonists are said to have sedative, analgesic, and euphoric effects.[10] DEX is a highly selective α2- adrenergic receptor agonist with a relatively high ratio of α 2/α 1 activity.[11] The hypnotic and supraspinal analgesic effects of DEX are mediated by the hyperpolarization of nonadrenergic neurons, which suppresses neuronal firing in the locus cereleus along with the inhibition of norepinephrine release and activity in the descending medullospinal noradrenergic pathway, secondary to the activation of central α2- adrenergic receptor.[12] DEX been used as intrathecal, epidural caudal for peripheral nerve blocks at dosages of 1–‒2 μg/kg, without causing any neurological deficits.[13,14] Bengisun *et al*. showed that addition of DEX to levobupivacaine for interscalene brachial plexus block decreases pain scores and increases patient satisfaction after arthroscopic subacromial decompression.[15] Whichever drug is injected in the regional space does get absorbed to some extent before finally getting metabolized, which most probably leads to its central sedative and analgesic effect.

On review of literature there is a study by Abdelhamid *et al*. who compared adding DEX as an additive to peribulbar block and intravenous DEX along with peribulbar block for cataract surgeries[16] and another study by Channabasappa *et al*., who used two doses of DEX in their study, i.e., 25 μg and 50 μg, added to the peribulbar block for cataract surgeries.[17] Ramaswamy *et al*. compared two doses of intravenous DEX (0.50 μg/kg.wt. and 0.25 μg/kg.wt.) and a combination of fentanyl midazolam for vitreoretinal surgeries.[18] However, to our knowledge, this is the first study using DEX in the peribulbar block for vitreoretinal surgeries. We have used a low dose of DEX similar to the dose used by Ghali *et al*. in subtenon's block, i.e., 20 μg.[19]

Abdelhamid *et al*. and Channabasappa *et al*. both showed that DEX added to the peribulbar block significantly shortened the onset of anesthesia and prolonged the duration of the anesthesia; however, in our study. it was found to have no statistically significant effect on the onset of anesthesia.[16,17] We did not study the duration of the anesthesia. However, we found the number of patients requiring block supplementation during the surgery was lower in the Dex group, but this was not statistically significant.

In our study, the mean sedation score was higher in the DEX group and the same was noted by Channabasappa *et al*. who found the mean sedation score to be higher in 50 μg Dex group than the 25 μg Dex group and the control group. The VAS scoring was lower in the in the DEX group at 5 min and at the completion of the surgery.

The surgeon satisfaction was found to be higher in the DEX group in our study. Ramaswamy *et al*. found surgeon satisfaction to be the maximum with 25 μg of DEX but it became lower when a higher dose of DEX (50 μg) was used or a combination of midazolam and fentanyl was used.[18]

In addition to the sedative effect, DEX has been reported in previous studies to have a stabilizing effect on BP and HR.[16-18,20] In our study, we found that the mean HR, DBP, and RR did not change significantly at different time points in the Dex group. There was significant change in the MAP and SBP in the Dex group, with a trend towards decrease in MAP and SBP leading to its stabilization. However, the SBP was significantly lower in the Dex group compared to the control group at the baseline.

In our study, we had no adverse events in the Dex group. However, 2 patients in the study by Abdelhamid *et al*. and 6 patients in the study by Channabasappa *et al*. developed bradycardia and were given atropine.[16,17]

Conclusion

To conclude, DEX was found to have sedative, analgesic, perioperative sympholytic, and hemodynamic stabilizing properties without causing any respiratory depression, and thereby making it a useful and safe adjunct to the peribulbar block in vitreoretinal surgeries increasing the surgeons' satisfaction by providing efficient pain relief, better sedation score, and greater stabilization of systemic parameters.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Sarvela PJ. Comparison of regional ophthalmic anesthesia produced by pH adjusted 0.75% and 0.5% bupivacaine and 1% and 1.5% etidocaine, all with hyaluronidase. Anesth Analg 1993;77:131-4.
2. Zahl K, Jordan A, McGroarty J, Sorensen B, Gotta AW. pH adjusted bupivacaine and hyaluronidase for peribulbar block. Anesthesiology 1990;72:230-2.
3. Memis D, Turan A, Karamanlioglu B, Pamukçu Z, Kurt I. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. Anesth Analg 2004;98:835-40.
4. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesth Analg 2010;111:1548-51.
5. Brummett CM, Padda AK, Amodeo FS, Welch KB, Lydic R. Perineural dexmedetomidine added to ropivacaine causes a dose dependent increase in the duration of thermal antinociception in sciatic nerve block in rat. Anesthesiology 2009;111:1111-9.
6. Kanazi GE, Aouad MT, Jabbour Khoury SI, Al Jazzar MD, Alameddine MM, Al Yaman R, *et al*. Effect of low dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006;50:222-7.
7. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: A critical review. Psychol Med 1988;18:1007-19.
8. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalonealphadolone. Br Med J 1974;2:656-9.
9. Weiss JL, Deichman CB. A comparison of retrobulbar and periocular anaesthesia for cataract surgery. Arch Ophthalmol 1989;107:96-8.
10. Jie K, van Brummelen P, Vermey P, Timmermans PB, van Zwieten PA. Identification of vascular postsynaptic alpha 1- and alpha 2-adrenoceptors in man. Circ Res 1984;54:447-52.
11. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (Bayl Univ Med Cent) 2001;14:13- 21.
12. Oda A, Lida H, Tanahashi S, Osawa Y, Yamaguchi S, Dohi S. Effects of alpha2adrenoceptor agonists on tetrodotoxin resistant Na+channels in rat dorsal root ganglion neurons. Eur J Anaesthesiol 2007;24:934-41.
13. Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, *et al*. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anaesthesiol Scand 2009;53:251-6.
14. She YJ, Zhang ZY, Song XR. Caudal dexmedetomidine decreases the required concentration of levobupivacaine for caudal block in pediatric patients: A randomized trial. Paediatr Anaesth 2013;23:1205-12.
15. Bengisun ZK, Ekmekçi P, Akan B, Köroglu A, Tüzüner F. The effect of adding dexmedetomidine to levobupivacaine for interscalene block for postoperative pain management after arthroscopic shoulder surgery. Clin J Pain 2014;30:1057-61.
16. Abdelhamid AM, Mahmoud A, Abdelhaq MM, Yasin HM, Bayoumi A. Dexmedetomidine as an additive to local anesthetics compared with intravenous dexmedetomidine in peribulbar block for cataract surgery. Saudi J Anaesth 2016;10:50-4.
17. Channabasappa SM, Shetty VR, Dharmappa SK, Sarma J. Efficacy and safety of dexmedetomidine as an additive to local anesthetics in peribulbar block for cataract surgery. Anesth Essays Res 2013;7:39-43.
18. Ramaswamy SS, Parimala B. Comparative evaluation of two different loading doses of dexmedetomidine with midazolam-fentanyl for sedation in vitreoretinal surgery under peribulbar anaesthesia. Indian J Anaesth 2016;60:89-93.
19. Ghali AM, Shabana AM, El Btarny AM. The effect of low-dose dexmedetomidine as an adjuvant to levobupivacaine in patients undergoing vitreoretinal surgery under sub-tenon's block anesthesia. Anesth Analg 2015;121:1378-82.
20. Ye W, Hu Z, Jin X, Wang P. Effects of dexmedetomidine for retrobulbar anesthesia in orbital ball implants after enucleation surgery. Indian J Ophthalmol 2015;63:704-9.