Research Paper

Effect of Addition of Fentanyl and Clonidine to Local Anesthetic Solution in Peribulbar Block

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Abstract

Objective: To compare the effect of addition of fentanyl and clonidine as adjuvants to bupivacaine and lignocaine in peribulbar block. **Methods:** The study was conducted on 105 adult patients of either sex, of ASA grade I and II undergoing ophthalmic surgeries. Patients were randomly divided into 3 groups of 35 each. All the patients were given peribulbuar block with 5ml lignocaine 2% +3 ml bupivacaine 0.5% +1 ml hyaluronidase (250 IU). In addition to this 1 ml normal saline was added to Group S, 25 µg fentanyl to Group F and 25 µg clonidine to Group C. Onset and duration of globe and lid akinesia, duration of sensory blockage and analgesia, hemodynamic parameters, number of rescue analgesic and visual analogue score were recorded. **Results:** The mean time of onset of globe and lid akinesia was significantly faster in group F and group C compared to group S, mean duration of globe and lid akinesia was longer in Group F (207.71 + 13.54 and 143.14 + 7.86 min) and group C (213.52 + 14.52 and 162.06 + 17.1 min) compared to group S (117.78 + 10.42 and 87.64 + 9.76 min). The mean duration of analgesia was significantly longer in group F (217.71 + 12.67) and C (258.82 + 14.50 min) as compared to group S (131.39 + 9.63 min). **Conclusion:** Addition of fentanyl or clonidine as adjuvant to local anaesthetic in peribulbar block provides faster onset and prolonged analgesia compared to local anaesthetic alone.

Keywords: Clonidine, fentanyl, peribulbar block, postoperative analgesia

Introduction

Regional anesthetic techniques with adjuvants are commonly used to improve block characteristics and extend analgesic effect into the postoperative period. For majority of ophthalmic procedures regional anesthesia in the form of peribulbar and retrobulbar block has gained popularity over general anesthesia.[1,2] The majority of patients are often elderly with comorbid conditions. There is less hemodynamic instability, less respiratory depression, better postoperative analgesia, and less nausea and vomiting with regional anesthesia and hence safer and more effective than general anesthesia.

Retrobulbar block provides adequate rapid anesthesia, akinesia and control of intraocular pressure as well as postoperative analgesia.[3-5] But sometimes, it may cause serious complications such as globe perforation, brainstem anesthesia, and retrobulbar hemorrhage. Peribulbar block is a rapid, simple and safe technique but requires larger volume of local anesthetic solution to produce the desired akinesia. The duration of the block depends on the type and composition of the local anesthetic mixture injected. Short duration of these blocks was found to be the main problem intraoperatively. Hence, the present study was carried out to determine effect of adding adjuvants to local anesthetic solution in peribulbar blocks for superior analgesia. The addition of adjuvant drugs such as opioids, clonidine, ketamine, and prostigmine to the local anesthetic mixture might prolong the duration of the block. These drugs have been used along with local anesthetics for extradural, intrathecal and peripheral nerve plexuses blocks to produce more intense and prolonged analgesia.[6-11] Opioids are commonly added to local anesthetic solutions to increase intensity and duration of anesthesia by acting on opioid receptors present on the central nervous system.[12,13] However, fentanyl has side effects like vomiting and respiratory

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depression.[10] Clonidine, an alpha 2-agonist, is found to prolong anesthesia and analgesia of local anesthetics and duration of retrobulbar block.[14] Bradycardia and hypotension are common side effects of clonidine.[15] Hyaluronidase as an adjuvant to anesthetic mixture helps in spreading injected mixtures thus accelerating the onset time and improving the quality of block.[16] The combination of fentanyl and clonidine added to local anesthetics has an advantage of decreasing the side effects of both the drugs due to smaller dose used.

Materials and Methods

After approval from Institutional Ethics Committee P. D. U. Medical College, Rajkot, a controlled prospective clinical study was carried out in the year 2014–2015 on 105 patients of age >15 years, of either sex including adult and geriatric age group undergoing ophthalmic surgeries under peribulbar block of the American Society of Anaesthesiology Grade I and II and informed written consent was obtained from all the patients. Exclusion criteria included-coagulation abnormalities, known allergic reaction to drug, local infection at the puncture site, patients with impaired orbital and periorbital sensation, patients with complicated vitreous hemorrhage as retinal detachment, extensive epiretinal membrane, dropped nucleus or intraocular lens, patients with posterior staphyloma, patients with axial length more than 28 mm or patient's refusal.

All the patients were made familiar with standard 10 cm visual analog scale (VAS) preoperatively.

For elimination of bias in the study blinding of investigators, participants, and assessors of both the study groups was done. Randomisation was done by computer-generated sequence numbers.

Three groups were made:

1. Control group S: 5 ml lignocaine 2% +3 ml bupivacaine 0.5% +1 ml hyaluronidase (250 IU) +1 ml normal saline
2. Fentanyl group F: 5 ml lignocaine 2% +3 ml bupivacaine 0.5% +1 ml hyaluronidase (250 IU) +1 ml fentanyl (25 μg diluted to normal saline 1 ml)
3. Clonidine group C: 5 ml lignocaine 2% +3 ml bupivacaine + 1 ml hyaluronidase (250 IU) +1 ml clonidine (25 μg diluted to normal saline 1 ml).

All patients underwent a preanesthetic check-up before surgery, and all the routine and specific investigations were documented. The patients were electively made nil per oral for 6 h before surgery. Standard monitors such as electrocardiogram, noninvasive blood pressure, and pulse oximeter were applied, and patients vitals were recorded, intravenous (IV) line was secured and patients were premedicated with injection glycopyrolate (0.2 mg IV, injection ondansetron (4 mg) IV and injection ranitidine (50 mg) IV.

Technique of peribulbar block

In peribulbar block, short beveled fine 25 G needle was inserted in inferotemporal part of lower orbital rim at the junction of medial 2/3 and lateral 1/3 at infraorbital notch. It was proceeded 1–2 mm vertically and tilted 15° superiorly, injecting local anesthetic mixture around the globe, total 10 ml of solution was injected, around 6–8 ml in peribulbar region and 2 ml in lower eyelid. Compression was given over the globe for 10 min with pinky ball (ball was released after first 5 min and then was compressed again to prevent central retinal artery occlusion).

Assessment of effect of block

Evaluation of the success of the block was done by scoring the mobility of eyeball at 1, 3, 5, 10, and 15 min after the end of injection. Movements were scored by three-point scoring system in the four quadrants as:

- 0 = akinesia (ocular movement <1 mm)
- 1 = reduced movement (ocular movement >1 mm but <4 mm)
- 2 = normal movement (ocular movement >4 mm).

Giving a maximum aggregate score of 8 for the four muscles, a score of 0 in all four directions was taken to indicate a successful block. If not achieved within 15 min after injection, the case was excluded from the study.

The onset of globe akinesia was recorded from the time of injection of local anesthetic until complete globe akinesia (Score 0).

Lid akinesia was assessed by asking the patient to open both the eyes widely followed by squeezing them maximally. Onset of lid akinesia was defined as time elapsing from injection of local anesthetic solution until complete lid paralysis.

Duration of globe akinesia was recorded from time of injection of local anesthetic mixture till recurrence of muscle movements (Score 8).

The duration of the lid akinesia was recorded from the time of injection of local anesthetic mixture till full recurrence of lid movements.

Globe anesthesia was assessed by a gentle touch on the conjunctiva with a cotton swab. Duration of globe anesthesia was recorded from the time of injection of local anesthetic till the complete disappearance of sensation.

The level of sedation was measured using Ramsay sedation score.

Ramsay sedation scale

1. Agitated, anxious or restless
2. Co-operative, oriented and tranquil
3. Responsive to commands only
4. Brisk response to light glabellar tap or loud auditory stimulus
5. Sluggish response to light glabellar tap or loud auditory stimulus
6. No response to light glabellar tap or loud auditory stimulus.

Postoperative assessment

1. Duration of lid and globe akinesia
2. Time of rescue analgesic given when VAS ≥4 and total number of rescue analgesic given.

Postoperatively, patients were monitored for pulse, blood pressure, SpO_2, sedation and complications (if any).

Assessment of pain

Patients were examined for the duration of analgesia as per VAS.

VAS is a 10 cm line which is marked as shown below.

The patients were asked to make a vertical mark on the line to indicate the intensity of their pain and VAS was scored by measuring from the left side, how far the patient marked towards the maximum pain end. This number was then used to compare changes in pain level. VAS was recorded hourly. When VAS of ≥4 postoperatively, rescue analgesia was given in the form of injection diclofenac sodium 1.5 mg/kg i.m. and time of rescue analgesia was noted.

All the patients were observed for incidence of any side effects and complications such as nausea, vomiting, hypotension, bradycardia, globe perforation, oculocardiac reflex, and chemosis during intra- and post-operative period.

Statistical analysis was done using Microsoft Excel 2010. Intergroup comparison of ordinal data was done by one-way analysis of variance. Categorical data were compared together using Chi-square test. $P < 0.05$ was considered statistically significant.

Results

Table 1 shows demographic characteristics of the three groups. There was no statistically significant difference among three groups in terms of age, weight, sex, and duration of surgery.

Table 2 shows the characteristics of the block. The mean time of onset of globe akinesia was significantly faster in group F (6.94 ± 3.55 min) and C (6.70 ± 3.3 min) as compared to group S (10.91 ± 3.74 min). Similarly, the mean time of onset of lid akinesia was significantly faster in group F (4.08 ± 1.73 min) and C (4.03 ± 1.72 min) as compared to group S (6.97 ± 3.61 min).

Mean duration of globe akinesia was 117.78 ± 10.42 min in group S, 207.71 ± 13.54 min in group F and 213.52 ± 14.52 min in group C signifying longer duration of globe akinesia in group F and C as compared to group S. Furthermore, the mean duration of lid akinesia was significantly longer in group F (143.14 ± 7.86 min) and C (162.06 ± 17.1 min) as compared to group S (87.64 ± 9.76 min).

Group F (217.7143 ± 12.67 min) and group C (258.82 ± 14.50 min) had a longer duration of analgesia in comparison to group S (258.82 ± 14.50 min). The mean duration of sensory blockage was longer in group F (79.71 ± 7.64 min) and C (80.88 ± 7.81 min) compared to group S (67.63 ± 7.925 min).

Figures 1 and 2 show hemodynamic changes during the surgery. Figure 1 shows the mean blood pressure changes during the surgery. In group S, mean blood pressure ranges from 90.9 ± 6.12 to 88.6 ± 15.5, in group F from 90.1 ± 4.92 to 88.3 ± 3.49, and in group C, it ranges from 92.2 ± 2.48 to 90.2 ± 4.34. There is no statistically significant difference in mean blood pressure of the patients between the three groups ($P \geq 0.05$).

Figure 2 shows the mean pulse rate changes during surgery. In group S, mean pulse rate ranges from 75.22 ± 8.94 to 76.82 ± 6.52, in group B from 78.62 ± 6.25 to 80.34 ± 6.34 and group C from 78.85 ± 3.37 to 81.33 ± 1.10. The result shows that there is no statistically significant difference in pulse rate of the patients between the three groups.

Figure 3 shows the first analgesic requirement after performing the block. Of 35 patients in group S, 11 patients required first

Table 1: Demographic characteristics (mean±standard deviation)

Characteristics	Mean±SD			*P*	Significance
	Group S	Group F	Group C		
Age (years)	59.22±10.71	59.39±14.40	55.41±15.04	0.06#	Not significant
Weight (kg)	57.55±7.44	57.23±10.40	55.53±8.94	0.61#	Not significant
Sex (male/female)	13/22	11/24	16/19	0.843*	Not significant
Duration of surgery (min)	16.42±3.28	16.43±3.29	16.52±2.8	0.84#	Not significant

*Chi-square test, #ANOVA. ANOVA=Analysis of variance, SD=Standard deviation

Table 2: Characteristics of the block

Characteristics	Mean±SD			*P*	Significance
	Group S	Group F	Group C		
Onset of globe akinesia (min)	10.91±3.74	6.94±3.55	6.70±3.3	<0.0001	Significant
Duration of globe akinesia (min)	117.78±10.42	207.71±13.54	213.52±14.52	<0.0001	Significant
Onset of lid akinesia (min)	6.97±3.61	4.08±1.73	4.03±1.72	<0.0001	Significant
Duration of lid akinesia (min)	87.64±9.76	143.14±7.86	162.06±17.1	<0.0001	Significant
Duration of analgesia (min)	131.39±9.63	217.7143±12.67	258.82±14.50	<0.0001	Significant
Duration of sensory blockage (min)	67.63±7.925	79.71±7.64	80.88±7.81	<0.0001	Significant

SD=Standard deviation

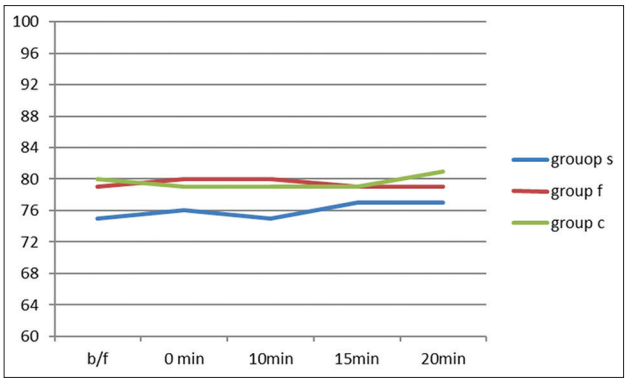

Figure 1: Pulse rate changes

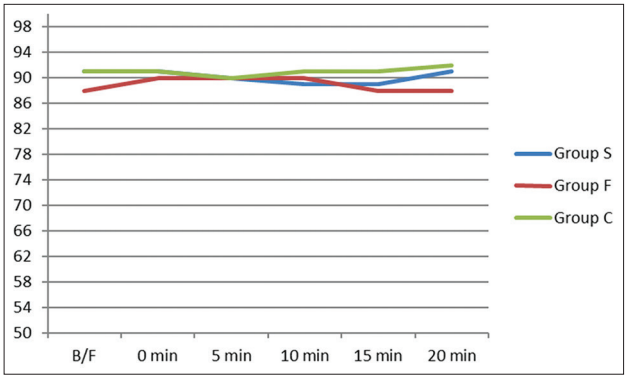

Figure 2: Mean arterial pressure changes

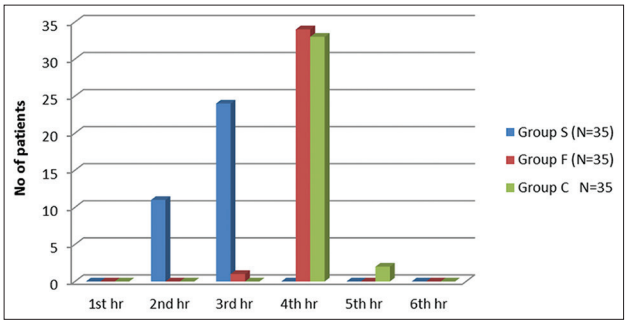

Figure 3: First analgesic requirement

analgesic dose in 2nd h and 24 patients required it in 3rd h. In group F 34 patients required the first analgesic in 4th h and only one required it in 3rd h. In group C, 33 patients required the first analgesic in 4th h and 2 required it in 5th h. These results show there is a longer duration of analgesia in group F and C as compared to group S.

Discussion

Injection of local anesthetic mixtures in neural blocks may sometimes lead to unsatisfactory surgical conditions for relatively lengthy operations. The addition of adjuvant to local anesthetics aims to prolong their duration of action. Opioids produce antinociceptive action by acting on central and peripheral opioid receptors.[17]

Local anesthetics act through blockage of selective sodium channels, on the other hand, opioids, act on opioid receptors and cause an increase in potassium conductance. Hence, the combination of local anesthetic and opioid provides superior anesthesia by inhibiting multiple areas of neuronal excitability. Fentanyl, a synthetic opioid has been shown to have local anesthetic action.[18-20] Clonidine is an alpha agonist with both analgesic and sedative properties. Its mechanism of action involves direct action on peripheral alpha 2 receptors and blockage of conduction of type C fibers.[20,21]

Our study compares the effect of the addition of fentanyl and clonidine to local anesthetic solution in peribulbar block. Results obtained in our study are comparable to study carried out by Maha MI oussef *et al*.[22]. They studied the effect of fentanyl versus that of clonidine when used as adjuvants to bupivacaine in peribulbar block and showed that the addition of either clonidine or fentanyl to the local anesthetic during peribulbar block results in a rapid onset and longer duration of the block with a longer period of postoperative analgesia (group F 262 min ± 9.71), group C 298 ± 11.16 min). The addition of clonidine was found to prolong the duration of the block more than that of fentanyl. Fahmy NG *et al*[23]. studied the effect of adding fentanyl and/or clonidine to local anesthetic on prolongation of the peribulbar block in cataract surgery and concluded that the addition of clonidine alone to local anesthetic solution in peribulbar block prolonged the duration of block for up to 2 h only. The addition of fentanyl alone to local anesthetic solution could not prolong the duration of the block, while the addition of both clonidine and fentanyl to local anesthetic solution prolonged the duration of the block for up to 3 h.

Prolongation of analgesia by clonidine is also supported by the study carried out by Bharti *et al*.[24] in which he added 1 µg/kg clonidine to local anesthetic mixture and found a significant increase in the duration of anesthesia and analgesia after peribulbar block.

Gupta and Gurunath[25] also showed that adding clonidine to local anesthetic mixture prolongs the duration of sensory blockage.

Our results are also consistent with the study done by Abo El Enin *et al*.[26] in which they studied the effect of fentanyl addition to local anesthetic in peribulbar block and observed that addition of fentanyl to local anesthetic mixtures fastens the onset and prolongs the duration of akinesia and postoperative analgesia in peribulbar block.

The study done by Connelly *et al*.[27] on the contrary reported no difference in the onset of akinesia after addition of clonidine. V. Toprek *et al*.[28] have also reported that addition of clonidine to 1% ropivacaine has no clinically significant benefit.

Apart from nausea and vomiting, chemosis was also reported in our study. A study by Bharti *et al*.[24] also showed no significant hemodynamic or respiratory side effects between the studied groups.

Further researches may be carried out for different doses of the adjuvants like clonidine and fentanyl to confirm the results of our study. Bharti *et al*.[24] compared the three doses of clonidine in peribulbar block and concluded that addition of 1 μg/kg clonidine with anesthetic mixture significantly prolonged duration of analgesia and anesthesia after peribulbar blocks with limited side effects.

Conclusion

Peribulbar block is a safe and effective technique for ophthalmic procedures. The addition of fentanyl or clonidine as an adjuvant to local anesthetic solution in peribulbar block provides faster onset and prolonged duration of globe and lid akinesia and postoperative analgesia with stable intraoperative hemodynamics.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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