

Comparison of peribulbar block and subtenon infiltration in pediatric enucleation for retinoblastoma

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Purpose: Enucleation performed in children with retinoblastoma is associated with severe postoperative pain. The use of opioids for the pain is associated with numerous complications which demand careful monitoring. Subtenon infiltration and peribulbar block are useful in ameliorating pain perioperatively following various ophthalmic surgeries which are yet to be evaluated in enucleation. Therefore, we designed this study to compare the effects of peribulbar block and subtenon infiltration on postoperative pain with opioids in pediatric enucleation surgeries. **Methods:** 60 children of American Society of Anesthesiologists grade I and II, age ranging from 6 months to 6 years with retinoblastoma undergoing enucleation surgery were included in the study. Group A ($n = 20$): received peribulbar block (peribulbar group); Group B ($n = 20$): received subtenon local infiltration (subtenon group); and Group C ($n = 20$): no block was given. **Results:** The postoperative fentanyl consumption was lowest with Group B compared to Group A and Group C (P value 0.001). However, the total fentanyl consumption was comparable between groups A and B, while it was significantly higher in the control group. The mean pain score face, legs, activity, cry, consolability (FLACC) scale and mean time to discharge from post anesthesia care unit were lowest in Group B followed by Group A, while Group C had the highest. There was no statistically significant difference among the 3 groups with regards to side effects. **Conclusion:** Subtenon infiltration showed significantly better outcomes when compared to peribulbar block and intravenous opioids alone without any untoward adverse effects.

Key words: Enucleation, peribulbar block, retinoblastoma, subtenon block

Retinoblastoma is a rare malignancy of the eye primarily affecting children, with an almost 95% mortality rate if left untreated.^[1,2] Enucleation is the primary mode of treatment for advanced retinoblastoma and retinoblastoma recalcitrant to chemotherapy, which is associated with severe postoperative pain.^[3] Perioperative analgesia is provided either with opioids or regional anesthesia. Although opioids are commonly used for analgesia, there is a gradual shift toward ophthalmic blocks owing to the side effects of opioids.

Peribulbar and subtenon blocks are useful in ameliorating pain following various ophthalmic surgeries like cataract surgeries, strabismus surgery, and vitreoretinal surgery.^[4-6] The complications like nausea, vomiting, and respiratory depression can be minimized while using ophthalmic blocks. The peribulbar block has been shown to reduce these complications in patients undergoing enucleation.^[7,8] However, there is currently no literature on the subtenon block in these patients.

Therefore, we designed this study to compare the effects of peribulbar block and subtenon infiltration on postoperative pain with opioids in pediatric enucleation surgeries.

Methods

We conducted a prospective randomized control study after approval by the institutional ethics committee and informed written parental consent. 60 children of American Society of Anesthesiologists (ASA) grade I and II, age ranging from six months to six years, with retinoblastoma scheduled for enucleation were recruited in the study and randomly allocated into three groups by computer-generated randomization table.

Group A ($n = 20$): Patients will receive peribulbar block after induction before the start of the surgery

Group B ($n = 20$): Patients will receive subtenon local infiltration at the end of enucleation with a primary ocular implant.

Group C ($n = 20$): Patients will not receive any block (control group).

Postoperative analgesia requirement measured by the number of rescue fentanyl boluses was the primary outcome. Secondary outcomes included Faces, Legs, Activity, Cry, Consolability (FLACC) scores at 0, 1, 2, 3, 4, 8, and 24 hours, time to first rescue analgesia postoperatively, intraoperative rescue analgesia requirements, postoperative ibuprofen

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requirements, postoperative nausea or vomiting (PONV), and oculocardiac reflex (OCR). Children whose parents were unwilling to give consent, children who were mentally challenged or deaf, and children with a history of allergy to local anesthetics were excluded from the study.

Anesthesia technique

All children received a standardized anesthesia technique. No premedication was given to any child. On being shifted to operation theater, the baseline values of oxygen saturation (SpO_2), heart rate (HR), noninvasive blood pressure (NIBP), and respiratory rate were recorded. Patients were induced either with propofol (3–5 mg/kg) if intravenous access was present or with 6%–8% sevoflurane in 100% O_2 . The airway was managed by a laryngeal mask airway (LMA) of appropriate size and was put on pressure-controlled ventilation. Anesthesia was maintained with O_2 /air/sevoflurane keeping end-tidal minimum alveolar concentration (MAC) 1. No muscle relaxant was given to any children.

Group A: Peribulbar block

In Group A, 0.3 ml/kg of a 1:1 mixture of 0.5% bupivacaine and 2% lignocaine with 5 IU/ml hyaluronidase was injected into the peribulbar space through the inferior eyelid at the junction of the lateral third and medial two-thirds of the inferior orbital rim. A single transcutaneous injection was performed using a 26 gauge 0.5-inch needle; the needle was directed vertically backward, parallel to the floor of the orbit. If contact was made with bone, the needle was redirected slightly upwards. The tip of the needle was kept extraconal, close to the orbital wall beyond the equator of the globe, but anterior to the posterior border of the globe, in the peribulbar space. After negative aspiration, the local anesthetic mixture was injected slowly.

Group B: Subtenon infiltration

In Group B, after induction of anesthesia, intravenous fentanyl 1 μ g/kg was administered. At the end of the procedure, local anesthetic infiltration through the anterior and posterior tenon layer was done using a 26 gauge 0.5-inch needle placing into the hole of the conformer using the same volume of the local anesthetic mixture (0.3 ml/kg of a 1:1 mixture of 0.5% bupivacaine and 2% lignocaine with 5 μ g/ml hyaluronidase).

Group C: Control group

In Group C, after induction of anesthesia, intravenous fentanyl 1 μ g/kg was alone administered. Continuous monitoring of ECG, SpO_2 , HR, NIBP, and end-tidal C_{O_2} was done intraoperatively and the patient was evaluated for perioperative analgesia. Analgesia was considered inadequate when there was a >20% rise in HR or BP over basal readings or requirement of sevoflurane >1.5% and was treated by intravenous fentanyl 0.5 μ g/kg. IV fentanyl was further repeated with a gap of at least 10 min between two doses. Intraoperative analgesia supplementation was noted. Incidence of any complication related to block was recorded. Incidence of OCR, defined as a sudden decrease in HR of more than 20%, or any arrhythmia during surgery was also recorded. At the end of the surgery sevoflurane and air was switched off and the LMA was removed after giving 100% O_2 . The child was then shifted to the post-anesthesia care unit (PACU) once the child was awake.

In the postoperative period, patients were assessed immediately (0 h), 1 h, 2 h, 3 h, 4 h, 8 h, and 24 h for pain and PONV. The pain was assessed by using the FLACC score. All pain assessments were done when the child was awake or responsive to minor stimulation. IV fentanyl 0.5 μ g/kg was administered for FLACC scores of more than 4 and repeated

after half an hour if required for 1st 4 hours. All children were kept for at least four hours in the PACU and shifted to the ward after achieving a modified Aldrete recovery score (MAS) of 9/10. Thereafter, children received syrup paracetamol 15–20 mg/kg 8 hourly, while syrup ibuprofen 10 mg/kg was administered for FLACC scores more than 4 as rescue analgesia. All children were observed for any PONV and were treated with Inj. ondansetron 0.1 mg/kg and requirement was recorded. Time to first rescue analgesia, the requirement of rescue analgesia, and rescue antiemetics along with the number of episodes of vomiting were also noted.

Statistical analysis

Statistical analysis was carried out by using IBM SPSS Version 22.0. Baseline characteristics were compared using Chi-square/Fisher's exact test for categorical data and one-way ANOVA for continuous variables. The intraoperative, postoperative, and total rescue fentanyl among the three groups were tested using one-way ANOVA, while intergroup comparisons were made using independent sample *t*-test. Postoperative pain assessed using FLACC score was analyzed by Wilcoxon-Mann-Whitney test. Time taken for first postoperative analgesia and time to discharge were analyzed by one-way ANOVA. Time to achieve MAS >9 within 30 min and after 30 min among the three groups were compared using the Chi-square test and Fisher's exact test. The incidence of PONV and OCR were compared using the Chi-square test and Fisher's exact test. Intergroup analysis between the groups was not done if the overall *P* value was >0.05. *P* value of <0.05 was taken to be statistically significant for all data in this study.

Results

A total of 64 children were enrolled in the study. Two of them refused consent and two were excluded from the study due to febrile episodes and lower respiratory tract infection on the day of surgery. The remaining 60 patients were randomized into 3 groups. Data from these patients were taken for analysis with SPSS Version 22.0. These data are represented in the CONSORT diagram [Fig. 1].

The demographic data of all 3 groups were found to be comparable when analyzed using the Kruskal-Wallis test [Table 1]. The intraoperative fentanyl consumption was comparable in groups (subtenon) B and (control) C with a mean of 2.15 ± 0.59 and 2.15 ± 0.67 respectively, while Group (peribulbar) A had the lowest consumption with a mean of 1.4 ± 0.50 (*P* value 0.001). The postoperative fentanyl consumption was lowest with Group B mean 0.3 ± 0.47 compared to peribulbar group 0.95 ± 0.83 and mean 1.65 ± 0.49 in the control group (*P* value 0.001). However, the total fentanyl consumption was comparable between groups A and B, while it was significantly higher in the control Group C with means of 2.35 ± 1.18 , 2.45 ± 0.61 , and 3.8 ± 0.83 , respectively (*P* value – 0.001) [Table 2]. The mean pain score (FLACC) in the immediate postoperative period was lowest in Group B (subtenon) with a mean of 1.5 ± 1.32 (*P* value –0.001) followed by Group A (peribulbar) with 2.7 ± 1.46 , while Group C (control) had the highest with a mean 4.35 ± 1.42 (*P* value – 0.001) [Table 3].

There was no statistically significant difference among the 3 groups with regards to nausea vomiting, rescue antiemetic consumption, and patient hemodynamics. However, more episodes of OCR were noted in the control and subtenon groups (*P* value 0.036). Incidence of OCR in Group A, B, and C are 10% (*n* = 2/20), 40% (*n* = 8/20), and 45% (*n* = 9/20) respectively [Table 4].

Meantime to discharge from PACU was 31.5 min (SD-9.75) in the peribulbar group compared to the subtenon group 24.5 min (SD-9.85) and 41.5 min (SD-13.77) in the control group, (P value = 0.001). Meantime to first postop analgesia consumption was 89.75 min (SD-60.67), 131.25 min (SD-58.17), and 48 (SD-65.84) in groups A, B, and C, respectively, P value 0.001 [Table 4].

None of the patients enrolled in the study suffered from dreadful complications like globe perforation, retrobulbar

hemorrhage, optic nerve damage, brain stem anesthesia, local anesthetic systemic toxicity, or myotoxicity. Only 2 patients in Group B (subtenon) had a minor subconjunctival hemorrhage.

Discussion

Retinoblastoma is a rare malignancy predominantly affecting children. However, it is the most common malignancy of the eye with an estimated incidence of 6000 to 8000 per year worldwide with mortality of almost 95% if untreated. Enucleation is the primary mode of treatment in advanced intraocular retinoblastoma and secondary after chemo reduction in extraocular retinoblastoma. With advanced multimodalities and better enucleation techniques, the survival rate has crossed 95% in these children when timely intervention is done.^[2]

Pain after enucleation is often very severe and to the child who has just lost vision from one eye aggravates the emotional component of pain. Assessment of pain in children is very difficult and complex. The emotional component of pain is a very strong determinant in children; hence, psychological support and proper preoperative parental counseling regarding the procedure are crucial.^[9] Peribulbar and subtenon blocks are useful in ameliorating pain following various ophthalmic surgeries.^[4-6] The complications associated with opioids can be minimized using these blocks.^[7,8]

The intraoperative fentanyl consumption was comparable in groups (subtenon) B and (control) C with a mean of 2.15 (SD-0.59) and 2.15 (SD-0.67), respectively, while Group (peribulbar) A had the lowest consumption with a mean of 1.4 (SD-0.50) (P value 0.001). This was expected because peribulbar block was performed at the beginning of the surgery, while subtenon block was given at the end of the surgery; thus, the intraoperative analgesic requirements were expected to be comparable in groups B and C, while Group A had a significantly lesser requirement of intraoperative fentanyl. This was in agreement with the previous report on the use of peribulbar analgesia in enucleation surgery by Calenda *et al.*^[8]

The postoperative fentanyl consumption was lowest with Group B 0.3 (SD-0.47) compared to peribulbar group 0.95 (SD-0.83) and 1.65 (SD-0.49) in the control group (P value 0.001). The mean FLACC score in the immediate postoperative period was lowest in Group B 1.5 (SD-1.32) (P value 0.001) followed

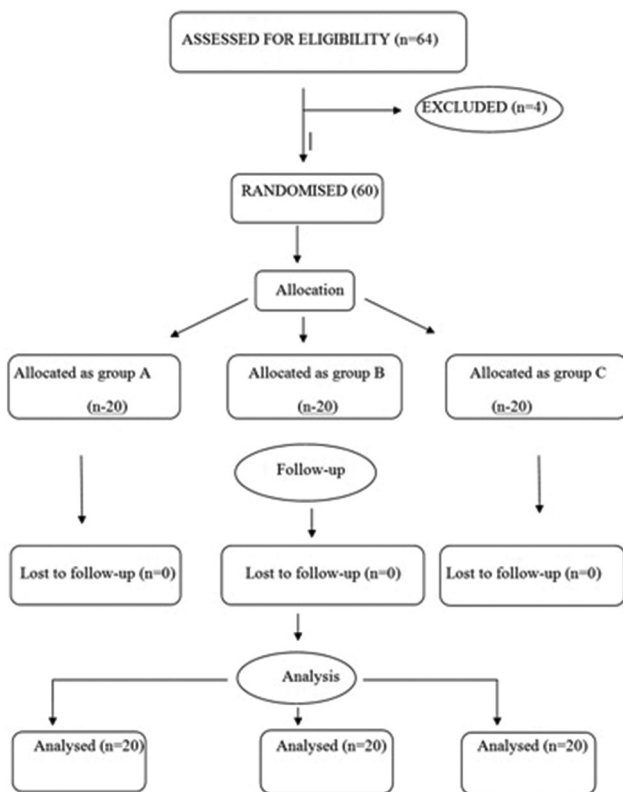


Figure 1: CONSORT flowchart

Table 1: Demographic profile

	Peribulbar (A)	Subtenon (B)	Control (C)	P
Age (Months) Mean±SD	28.20±19.64	27.20±17.18	25.65±16.13	0.9
Sex M:F	07:13	12:08	11:09	0.247
Weight (Kg) mean±SD	12.6±3.39	11.65±3.45	10.8±3.05	0.235
ASA status	1	1	1	1
Diagnosis R:L	10:10	10:10	09:10	0.935

Table 2: Analgesic requirement

	Peribulbar (A)	Subtenon (B)	Control (C)	P
Intraoperative rescue fentanyl	1.4±0.50	2.15±0.59	2.15±0.67	0.001
Postoperative rescue fentanyl	0.95±0.83	0.3±0.47	1.65±0.49	0.001
Total rescue fentanyl	2.35±1.18	2.45±0.61	3.8±0.83	0.001
Postoperative ibuprofen	0.45±0.51	0.5±0.607	1.05±0.69	0.004
Postoperative paracetamol	3	3	3	1
Time to first postoperative analgesia (min)	89.75±60.67	131.25±58.17	48±65.84	0.001

*The values mentioned above are total number of times bolus were given, hence no values/units denoted

by Group A 2.7 (SD-1.46), while Group C (control) had the highest 4.35 (SD-1.42) (*P* value – 0.001). The lower requirement and better pain scores in the subtenon group were probably because the subtenon block was performed at the end of the surgery, thereby having a greater effect in the immediate postoperative period than groups A and C. However, the total fentanyl consumption was comparable between groups A and B, while it was significantly higher in the control Group C with means of 2.35 (SD-1.18), 2.45 (SD-0.61), and 3.8 (SD-0.83), respectively (*P* value – 0.001). This suggests that the overall efficacy of the two regional techniques was comparable and better than the usual care with i.v. opioids alone.

Yen *et al.*^[7] collected data from anesthetic records of 39 adult patients who underwent enucleation surgery, out of which 21 patients received periocular anesthesia and 18 patients received general anesthesia. A lesser number of patients in the periocular anesthesia group required rescue analgesics. PONV scores were also significantly lesser in the periocular anesthesia group. This was in accordance with our study with both groups A and B having reduced pain score and analgesic requirements. Subramaniam *et al.*^[10] studied 85 patients undergoing pediatric vitreoretinal surgery. They administered peribulbar block to 42 patients and the rest received pethidine. They found that patients who received the block had less PONV and also required less opioids in the postoperative period. They also found that children who received peribulbar block had a lesser incidence of OCR. This was in agreement with our study where a higher number of episodes of OCR were noted in the control and subtenon groups (*P* value 0.036). Incidence of OCR in Group A, B, and C are 10% (*n* = 2/20), 40% (*n* = 8/20), and 45% (*n* = 9/20), respectively. OCR is a trigeminal vagal reflex

caused by pressure on the eyeball, traction of extra-ocular muscles, orbital hematoma, and trauma. Repeated stimulation might cause fatigue to this reflex arc at the level of the cardioinhibitory center leading to a reduction in the incidence of subsequent OCR. It can manifest as bradycardia, nodal rhythm, ectopic beats, ventricular fibrillation, or asystole.^[11]

Ghai *et al.*^[5] compared the efficacy of subtenon with intravenous fentanyl in 114 children subjected to pediatric cataract surgery. They found that there was a significant decrease in postoperative pain and vomiting, along with a lesser incidence of OCR in the subtenon block group. 63 infants undergoing pediatric cataract surgery were divided into two groups by Sethi *et al.*^[12] One group received subtenon block and the other group received intravenous fentanyl. The rescue analgesic requirement and PONV were significantly lower in children who received subtenon block. Gupta *et al.*^[13] compared the complications with peribulbar block and topical local anesthetic application in 45 children undergoing pediatric strabismus surgery. They found that PONV was reduced in both groups when compared with general anesthesia alone. OCR was significantly reduced in the peribulbar block group. Calenda *et al.*^[8] administered peribulbar block and local anesthetic filled implant to 115 adult patients undergoing enucleation and found that the combination of local anesthetic techniques provided postoperative analgesia for a variable number of hours.

Calenda *et al.*^[3] studied the efficacy of subtenon infiltration of local anesthetic at the end of surgery for providing postoperative analgesia in patients undergoing posterior segment surgery under general anesthesia. They found that subtenon infiltration resulted in excellent pain relief that lasted for about six hours. They concluded that subtenon infiltration is a highly reliable and safe method of providing postoperative analgesia. The decrease in pain scores and analgesic requirements are in agreement with our study; however, the higher incidence of OCR in the subtenon group can be attributed to the timing of the block as it was given at the end of the surgery.

PONV is one of the most common complications seen after pediatric ophthalmic procedures. It is one of the leading causes of parental dissatisfaction after surgery and unanticipated hospital admission following ambulatory surgery with resulting increased health care costs.^[14] It is desirable to prevent this issue so as to reduce postoperative morbidity. Repeated vomiting can affect the integrity of suture, increase the cost

Table 3: FLACC scores

	Peribulbar (A)	Subtenon (B)	Control (C)	<i>P</i>
*FLACC 0	2.7+1.46	1.5+1.32	4.35+1.42	0.001
FLACC 1	2.2+0.77	1.5+0.61	2.8+0.77	0.001
FLACC 2	1.05+0.61	0.50+0.61	1.85+0.75	0.001
FLACC 3	1.05+0.69	1.1+1.02	2.9+1.5	0.001
FLACC 4	1.15+0.37	1.15+0.81	2.95+1.36	0.001
FLACC 5	0.8+0.62	0.85+0.67	1.4+0.6	0.008

*FLACC scale denotes Face, Legs, Activity, Cry, Consolability scale and 0, 1, 2, 3, 4, and 5 denote 0, 1, 2, 3, 4, and 8 hours, respectively

Table 4: Side effects, time to discharge, and MAS

Groups	Peribulbar (A)	Subtenon (B)	Control (C)	<i>P</i>
*NV0 yes: no	03:17	07:13	11:09	0.116
*NV1 yes: no	02:18	04:16	06:14	0.287
*NV2 yes: no	00:20	03:17	02:18	0.217
*NV3 yes: no	00:20	03:17	02:18	0.217
*NV4 yes: no	00:20	00:20	00:20	1
*NV5 yes: no	00:20	00:20	00:20	1
*NV6 yes: no	00:20	00:20	00:20	1
Rescue Analgesia yes:no	05:15	08:12	07:13	0.592
*OCR yes: no	02:18	08:12	09:11	0.036
Time to discharge (min)	31.5±9.75	24.5±9.85	41.5±13.77	0.001
*MAS <30 min: >30 min	10:10	15:05	06:14	0.017

*NV denotes postoperative nausea and vomiting; OCR: oculocardiac reflex; MAS: modified Aldrette score; and 0, 1, 2, 3, 4, 5, and 6 denotes 0, 1, 2, 3, 4, 8, and 24 h, respectively

of antiemetic drugs, and prolong the postoperative stay.^[15] The incidence of PONV in our study was comparable in all the groups, our results were comparable with the previous study conducted in pediatric strabismus surgery.^[13] They demonstrated no significant difference among the groups receiving ophthalmic blocks.

Our findings differ from the results of the study conducted by ramachandran *et al.*^[16] which compared the analgesic efficacy of intravenous fentanyl with subtenon block in squint surgery. Their study did not demonstrate much difference in the analgesic efficacy. This difference in the outcome from our study could be possibly due to the difference in the age group operated (Mean 6-7 years), type of surgery- strabismus, opioids dosage and pain score(CHEOPS) used. We believe that more painful surgeries like enucleation with extensive surgical manipulation can benefit from subtenon infiltration.

Nonpharmacological role of management of pain in infants and small children like swaddling, use of pacifiers, suckling, feeding with breast milk,^[17] usage of dextrose solutions,^[18] and skin-to-skin care^[19] plays a very important role as suggested by recent Cochrane database reviews. All the infants and small children enrolled in this study were nursed in the mother's lap in the immediate postoperative period and provided with skin-to-skin care and were started on early breastfeeding.

Shende *et al.*^[20] conducted a study comparing the efficacy of peribulbar block (0.25% bupivacaine) with intravenous morphine in 60 ASA-grade I patients undergoing retinal detachment repair surgery. Our results were comparable with this study, where patients who received blocks had better pain relief, faster discharge and recovery score (*P* value 0.0001). Our results were also comparable to the study conducted by Elgohary and Hosny^[6] which was done in 40 children of the 6-12 age group undergoing ophthalmic surgeries. Their study pointed out the efficacy of peribulbar block in better postoperative outcomes, pain scores, and faster recovery.

Meantime to discharge from PACU was 31.5 min (SD-9.75) in the peribulbar group compared to the subtenon group 24.5 min (SD-9.85) and 41.5 min (SD-13.77) in the control group, (*P* value = 0.001). Meantime to first postop analgesia consumption was 89.75 min (SD-60.67), 131.25 min (SD-58.17), and 48 (SD-65.84) in groups A, B, and C, respectively, *P* value 0.001. Patients who received intravenous fentanyl as a primary mode of analgesia consumed rescue analgesia earlier than those patients who received subtenon block and peribulbar block. This is in accordance with previous studies which demonstrated a significant delay in time for the first analgesic requirement and early time to discharge in those patients who received ophthalmic blocks.^[5]

Conclusion

Subtenon infiltration in enucleation surgeries shows a significantly better pain relief, less pain scores in the immediate postop period, a faster discharge from PACU, and delayed first postop analgesic consumption when compared to peribulbar block and intravenous opioids alone without any untoward adverse effects in children with retinoblastoma undergoing enucleation. However, we suggest, a risk-benefit ratio should be assessed well before instituting these procedures in children for a minimally invasive, less painful procedure like cataract surgeries after achieving adequate expertise in adult patients.

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Conflicts of interest

There are no conflicts of interest.

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