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# Dexmedetomidine *vs.* Fentanyl as Adjuvant to Local Anaesthetic Mixture in Peribulbar Block for Retinal Surgery: A Randomized Prospective Study

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## Abstract

**Background and aims:** we aimed to compare the effects of adding dexmedetomidine *vs.* fentanyl as adjuvants to local anesthetic mixture in peribulbar block for retinal surgery.

**Methods:** One hundred and thirty adult patients scheduled for retina surgery under peribulbar block were included in this prospective randomized study. The study included 2 groups: Group D received local anesthetic mixture (bupivacaine 0.5%+lidocaine 2%+hyaluronidase 15 IU/mL) plus 20 μg of dexmedetomidine I and Group F received the same local anesthetic mixture plus 20 μg of fentanyl. We observed the onset and duration of sensory and motor block, number of patients needed supplemental local anesthetic injection, volume of anesthetic injected, Ramsay sedation score, visual analogue scale for pain, and adverse events.

**Results:** Dexmedetomidine group was associated with significantly decreased onset of sensory (1.69 ± 0.64 sec *vs.* 2.23 ± 0.66 sec) (P<0.05) and motor block (7.23 ± 2.52 sec *vs.* 8.83 ± 2.10 sec) (P<0.05) and prolonged duration of sensory (162.11 ± 6.66 sec *vs.* 148.02 ± 5.45 sec) (P<0.05) and motor block (186.97 ± 10.33 sec *vs.* 157.55 ± 4.38 sec) (P<0.05). Dexmedetomidine group showed significantly higher sedation score for one hour and better postoperative analgesia with significantly lower paracetamol consumption and fewer patients requiring naluphin as rescue analgesia. Number of patients needed supplementary injection and the total injected anesthetic volume were significantly higher in fentanyl group compared to dexmedetomidine group.

**Conclusion:** Adding Dexmedetomidine to peribulbar block for retinal surgery was superior to adding fentanyl as Dexmedetomidine was associated with better block, more sedation and analgesia, and less analgesic requirement.

**Keywords:** Dexmedetomidine; Fentanyl; Peribulbar block; Retinal surgery

## Introduction

Regional block (especially peribulbar block) is the preferred choice of anesthesia for many ophthalmic surgeries as it has less complications [1].

Retinal surgery presents a multitude of problems to the anesthesiologists as it has long duration with high incidence of postoperative pain and most of the patients are old age with multiple systemic diseases [2].

Peribulbar block with local anesthetics only lead to delayed onset corneal anesthesia and globe akinesia, and frequent need of block supplementation. Anesthesiologists added many drugs to local anesthetics to improve the quality of the block but with limited success [3,4].

Fentanyl (Hameln pharmaceutical, Germany) is an opioid that can be added to local anesthetics to decrease the onset time and prolonged the duration of the block [5].

Dexmedetomidine (Pfizer, USA) is a new drug which belongs to alpha 2 adrenergic receptor agonist. When added to local anesthetics, alpha 2 adrenergic receptor agonist (as Dexmedetomidine and clonidine) is proved to improve the quality of the block [6].

The aim of this study was to evaluate and compare the effects of adding dexmedetomidine *vs.* fentanyl as adjuvants to Lidocaine 2%, Bupivacaine 0.5%and hyaluronidase mixture in peribulbar block for retinal surgery.

## Methods

This randomized prospective double blinded study (both patients and anesthesiologists who injected local anesthesia and collect data were blinded to the drug used) was carried out in Tanta University Hospital for 6 months (from June to December 2016) on 130 adult patients (ASA I -III) of both sex, aged 40-80 years scheduled for elective retinal surgery under peribulbar block after approval by the institutional ethical committees. Each patient signed a written and informed consent.

Patients were excluded from the study if they had active ocular infection, were single eyed, refused local anesthetics, were allergic to bupivacaine and lidocaine, could not lie flat, or had history of coagulopathy.

No premedication, topical anesthetic or intravenous sedative medications were used before or during the block. Supplemental $O_2$ at 2 L/min via nasal cannula was used throughout the procedure.

Patients were randomized into two equal groups (each 65 patients).

**Group D:** Received Bupivacaine 0.5%+lidocaine 2%+hyaluronidase 15 IU/mL+20 µg of dexmedetomidine.

**Group F:** Received Bupivacaine 0.5%+lidocaine 2%+hyaluronidase 15 IU/mL+20µg of fentanyl.

Block randomization was done using a computer system (www.randomization.com) to create a list of number, each number referred to one of the two groups. Then opaque envelope was used to seal each number. Then the patient was asked to choose one of the envelopes and gave it to the anesthesiologist who compared the number with computer generated list and accordingly scheduled the patient to one of the 2 groups. This anesthesiologist is the one who prepared the anaesthetic solution plus the studied drug, labeled it, and gave it to another anesthesiologist who gave peribulbar block and collected the data while he was blinded to the content of the syringe.

## Technique of block

After arrival of the patient to operating room, peripheral intravenous (IV) cannula was inserted. Standard monitoring, including electrocardiogram (ECG), noninvasive arterial blood pressure, and peripheral oxygen saturation ($SpaO_2$) was used. The eyelids and the surrounding area were cleaned with betadine 5% solution. Nine ml of anesthetic solution was taken (4cc lidocaine 2%+4 cc of bupivacaine 0.5% plus hyaluronidase 15 IU/mL+1cc of the study drug in a 10 cc syringe). The needle which was used is a 25-gauge, 5/8 inch. The needle was inserted and advanced as described by Rizzo et al. [7], then after negative aspiration (to avoid intravascular injection) local anesthetic was injected. A Honan balloon (set at 30 mm Hg for 10 min) was used for mechanical compression of the orbit.

An observer who was blinded to the aim of the study assessed all the measures.

**Primary outcome:** Primary outcome was the duration for motor block.

**Secondary outcome:** Secondary outcome included number of patients who need supplement (akinesia score>3 after 10 min), total volume for local anaesthesia drugs, onset time for sensory block, duration of sensory block, onset time for motor block, Ramsay Sedation Score [8], first time request analgesia, total paracetamol consumption, and number of patients requiring naluphine.

Akinesia of extraocular muscles was evaluated every 2 min in each of the 4 direction (superior, inferior, lateral and medial) using a 3-point scoring system: 2=normal movement; 1=partial akinesia; 0=complete akinesia, giving an aggregated score ranging from 0 to 8 for the 4 direction. Successful block was defined as an akinesia score of 3 or less (not more than 1 in each direction) [9]. Three to five ml of local anaesthetic mixture (Supplementary anaesthesia) was injected either superiorly (if the movement was lateral or superior)or medially (if the movement was medial or inferior) if the motor blockade was inadequate after 10 min of the block and the total volume of local anesthetic solution injected (mL) was calculated. Onset of Sensory block (time from injection of local anesthetic to loss of corneal sensation) was detected by ablation of corneal reflex in response to touching cornea with cotton wick every 30 second (sec). The duration of sensory block (the time from loss of corneal sensation till return of corneal sensation) and the duration of motor block (the time started from maximum akinesia till eyes move freely), were determined by frequent examination in the postoperative period every 30 min.

Sedation level was assessed by Ramsay Sedation Score every 15 min for 2 h after injection of local anesthetics then every 30 min for another 2 h.

The Patient's level of pain was assessed at 1 h, 2 h, 4 h, 6 h, 8 h, 12 h, and 24 h postoperatively using Visual analogue scale (0=no pain to 10=worst pain). If the VAS is >3, paracetamol l0 mg/kg was given intravenous. If the patient complained of severe pain (VAS is >7) naluphin 10 mg (in addition to paracetamol) was given intravenously as rescue analgesia medication. For both analgesics the maximum frequency was 6 h, and the maximum number of doses/24 h was 3 doses. Total paracetamol consumption (mg), number of patients (%) required naluphin as rescue analgesia, and time of first request for analgesia were recorded. Any adverse effects as respiratory depression (respiratory rate<10/min), oxygen desaturation ($SPO_2$<92%), bradycardia (HR<50 beats/min), and hypotension (MAP <50 mmHg sustained for more than 10 min), were recorded.

**Power of the study:** A previous study reported that the mean duration of the motor block was 179 min ± 27.69 [10]. Based on this study, 64 patients in each group was required to detect a statistically significant difference between groups in our primary outcome parameter, assuming an alpha error of 0.05 and power of 80%. We aimed to study 65 patients in each group (Figure 1).
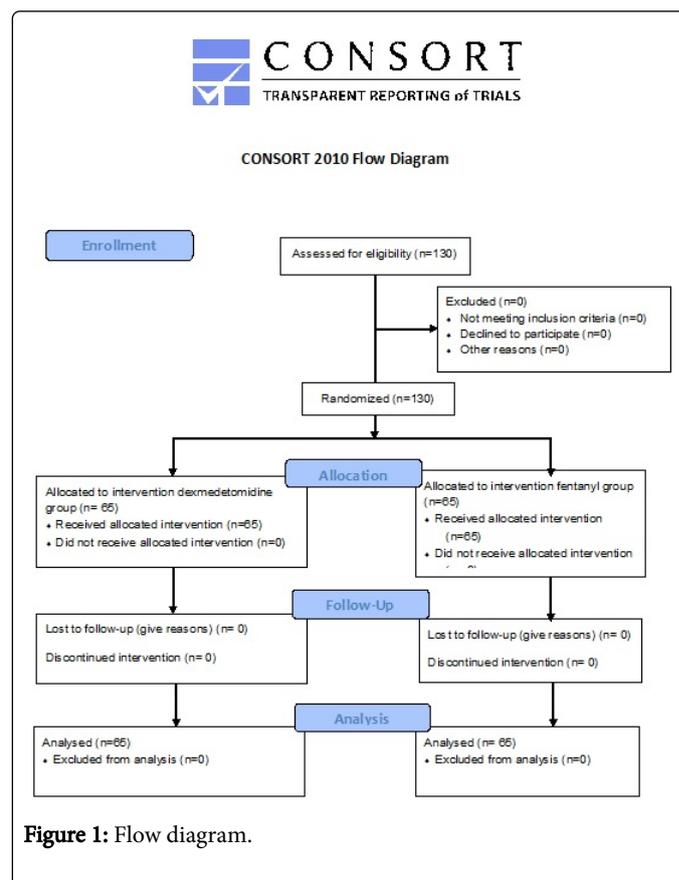


**Figure 1:** Flow diagram.

## Statistical analysis

Statistical analysis was done using SPSS 20 programme (IBM, Armonk, NY, United States of America).

Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

Independent-samples t-test of significance and Chi-square ($\chi^2$) test of significance were used to compare qualitative data and qualitative data respectively.

## Results

Regarding age, sex, weight and duration of surgery no significant differences were detected between both groups (Table 1).

|  | Group( D) | Group (F) | P value |
|---|---|---|---|
| **Age (years)** | 60.87 ± 9.5 | 60.47 ± 8.8 | 0.805 |
| **Weight (kg)** | 73.76 ± 6.2 | 75.4 ± 5.3 | 0.133 |
| **Sex (M/F)** | 40/25 | 45/20 | 0.19 |
| **Duration of surgery (min)** | 87.15 ± 8.5 | 90.09 ± 10.4 | 0.08 |

Data are presented as mean ± SD.

(* ) significant differences between groups (P<0.05).

**Table 1:** Patients' characteristic.

The number of patients who need supplemental local anesthetic and the total volume of local anesthetics used were significantly higher in group (F) as compared to group (D) (P<0.003 and 0.001 respectively).

Dexmedetomidine group (D) showed significantly shorter onset time of both sensory block and motor block as compared to Fentanyl group (F). The duration of both sensory block and motor block were significantly longer in Dexmedetomidine group (D) compared with fentanyl group (F) (Table 2).

|  | Group (D) | Group (F) | P value |
|---|---|---|---|
| **Number of patients who need supplement (akinesia score > 3 after 10 minutes)** | 7/65 (10.8%) | 21/65 (32.2%) | 0.003* |
| **Total volume for local anaethesia drugs (ml)** | 9.32 ± 0.94 | 10.06 ± 1.80 | 0.001* |
| **Onset for sensory block (min)** | 1.69 ± 0.64 | 2.23 ± 0.66 | 0.001* |
| **Duration of sensory block (min)** | 162.11 ± 6.66 | 148.02 ± 5.45 | 0.001* |
| **Onset time for motor block (min)** | 7.23 ± 2.52 | 8.83 ± 2.10 | 0.001* |
| **Duration of motor block (min)** | 186.97 ± 10.33 | 157.55 ± 4.38 | 0.001* |

Data are presented as mean ± SD or number and ratio.

(* ) significant differences between groups (P<0.05).

**Table 2:** Operative Data.

Both groups showed no serious complication (Table 2).

Dexmedetomidine group (D) showed significantly longer time to request analgesia (for the first time) as compared with group (F) (P=0.001). Also the number of patients who need naluphin as rescue analgesia and the total paracetamol consumption were significantly higher in group (F) compared to group (D) (P<0.001 and 0.001 respectively) (Table 3).

|  | Group(D) | Group (F) | P |
|---|---|---|---|
| **First time request analgesia (min)** | 290.28 ± 29.97 | 168.97 ± 9.38 | 0.001* |
| **Total paracetamol consumption** | 161.85± 285.68 | 370.77 ± 337.49 | 0.001* |
| **Number of patients requiring naluphine** | 9/65 (13.8%) | 46/65 (70.8%) | 0.001* |

Data are presented as mean ± SD or number and ratio.

(*) significant between groups (P<0.05)

**Table 3:** Postoperative data.

Group (D) showed significantly higher sedation score as compared to group (F) during the first hour after the block (P<0.05), but after one hour both groups were comparable regarding sedation score (Figure 2).
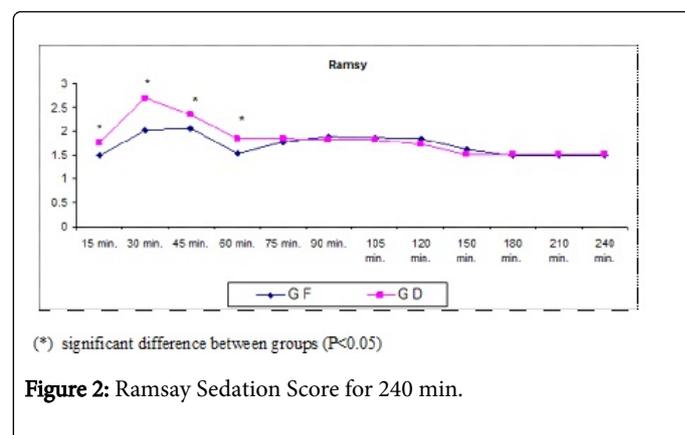


(*) significant difference between groups (P<0.05)

**Figure 2:** Ramsay Sedation Score for 240 min.



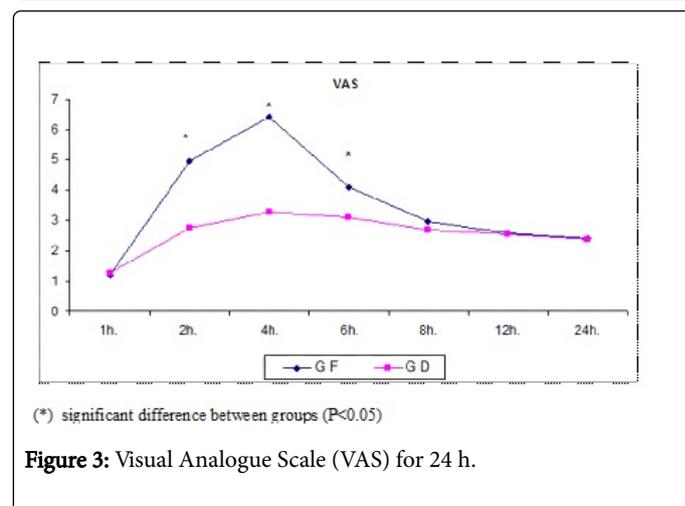(*) significant difference between groups (P<0.05)

**Figure 3:** Visual Analogue Scale (VAS) for 24 h.

Visual analogue scale was significantly higher in group (F) than group (D) at 2, 4, and 6 h postoperative but both groups were comparable at 8, 12, and 24 h postoperative(P<0.05) (Figure 3).

No significant differences were detected between groups in the mean arterial blood pressure, HR or $SPO_2$ after injection of local anesthetic at any time-point in the study (data not represented).

## Discussion

To the best of our knowledge few studies evaluated the addition of dexmedetomidine or fentanyl to local anesthetic drugs for peribulbar block but no study compare between the effect of the two drugs on peribulbar block.

Our study showed that when we compared adding dexmedetomidine *vs.* fentanyl to local anesthetic drugs for peribulbar block, dexmedetomidine group was associated with rapid onset and prolonged duration of sensory and motor block and provided better sedation and postoperative analgesia (at 2 h, 4 h, and 6 h postoperatively) with lower paracetamol consumption and fewer patients requiring naluphin as rescue analgesia.

Dexmedetomidine increases the effect of local anesthetics and prolongs their duration of action through peripherally or centrally mediated action. Peripherally, α2-agonists produce analgesia by reducing the release of norepinephine and causing inhibitory effect on nerve fiber action potential resulting in analgesia. Centrally, α2-agonists activate α2-adrenoreceptor and inhibit substance P release in the nociceptive pathway at the level of the dorsal root neuron resulting in sedation and analgesia [11-14].

Opiates as fentanyl mediate its analgesic effect though central opioid receptor in the brain and spinal cord [15] and though its direct action on the peripheral opioid receptors (including opioid receptors on primary afferent fibers), [16,17], and thus improves the quality of regional anaesthesia when added to local anesthetics. Also, fentanyl was found to have a local anesthetic action [18].

Our result was in line with the study carried by Channabasappa et al. [10], who added dexmedetomidine to local anesthetics used for peribulbar anesthesia and reported that adding dexmedetomidine shortens the onset time and prolongs the duration of sensory and motor block, and produces sedation. Poonam Nehra et al. [19] compared the addition of fentanyl *vs.* clonidine (alpha 2 agonist) to local anaesthetic mixture during peribulbar block and reported that the onset time of globe akinesia was significantly shorter in fentanyl group (F) and clonidine group (C) compared to control group (S). They also reported that the durations of motor block and analgesia were significantly longer in Group F and group C compared to group S. On the other hand Hala et al. [4] , reported that adding clonidine to local anesthetics for peribulbar block was associated with insignificant difference regarding onset time for sensory and motor block (which disagreed with our result) and improvement in the duration and the quality of the block (which agree with our results).

Our results were supported by other studies which reported that adding dexmedetomidine to local anesthetics for nerve block was associated with improvement of the block quality [20,21].

Our result recorded that Ramasy sedation score was higher in group (D) than group (F), sedation score was 3 during the first hour without any side effect or haemodynamic changes and this makes the patients more comfortable during the surgery with arousable sedative effects

which decreased with time. This result is support by the study done by Channabasappa et al. [10], who recorded that there was a significant increase in modified Ramsay score when he used dexmedetomidine in two doses (25 μg, 50 μg) added to local anesthetics used for peribulbar block.

## Limitation of the Study

There was no control group but previous studies proved that both studied drugs potentiate the effect of local anaesthesia. The other point was the dose of dexmedetonidine and fentanyl, we used doses close to that used in previous studies but the exact dose to give the best result is not clear and this may be a point for future research. We think that the previous 2 limitations did not affect the strength of the study.

## Conclusion

Adding Dexmedetomidine to peribulbar block for retinal surgery was superior to adding fentanyl as regards onset and duration of sensory and motor block, supplementary injection of local anesthetic, the total injected anesthetic volume, sedation score, postoperative analgesia, and analgesic requirement.

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