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Research Article

Comparing different fentanyl concentrations added to local anesthetic mixture in peribulbar block for cataract surgery

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KEYWORDS

Fentanyl;
Local;
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Abstract *Objective:* Evaluation of the effect of different concentrations of fentanyl added to the local anesthetic mixture on the onset and duration of globe anesthesia, after peribulbar block, with the least side effects.
Design: Double blinded randomized controlled clinical trial.
Setting: Kasr Al Aini hospital, Cairo University.
Methods: 60 patients with cataract grade 1–3 in the age group 40–70 years, with American Society of Anesthesiologists (ASA) grade I, II and III, scheduled for elective cataract surgery under regional anesthesia. They were randomly divided into four groups: in Group 1 (Control Group), patients received Lidocaine 2% and Hyaluronidase 15 IU/ml; in Groups 2, 3 and 4 (Fentanyl Groups), the patients received Lidocaine 2% and Hyaluronidase 15 IU/ml in addition to Fentanyl 1 μg/ml, 2 μg/ml and 3 μg/ml respectively. The onset and duration of lid and globe akinesia were assessed. Postoperative Visual Analogue Score was recorded each hour up to 6 h.
Results: No statistical significant difference was observed between the four groups in the onset and duration of lid and globe akinesia. There was a significant difference between the control group and the fentanyl groups as regards the duration of analgesia that was significantly prolonged in the groups that received fentanyl at concentrations of 2 μg/ml and 3 μg/ml in these group patients required analgesia after 116 ± 19 min and 144 ± 11 min respectively compared to the control group and the group that received fentanyl at a concentration of 1 μg/ml group who required analgesia after 100–103 min.
Conclusion: Adding Fentanyl at concentrations ⩾ 2–3 μg/ml to the local anesthetic mixture (Lidocaine and Hyaluronidase) for regional peribulbar block provides safe and effective method in improving postoperative analgesia in patients undergoing cataract surgery.

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1. Introduction

Retrobulbar and peribulbar regional anesthetic blocks are considered the two main approaches in the eye that can provide suitable surgical and medical conditions for intraocular surgeries, especially in elderly patients [1]. Cataract surgery requires a potent motor blockade of the eye globe and eyelids [2]. Despite the adequate rapid anesthesia and akinesia that can be provided by retrobulbar block, Peribulbar block became more widely used due to its ability to provide the same anesthetic effect with lower rate of complications [3]. Injection of local anesthetic mixtures only may provide unsatisfactory surgical conditions as regards the block intensity and duration especially for relatively lengthy operations. So, additive drugs such as opiates, may improve the quality of the block and provide good postoperative analgesia [4–6].

Opiates are known to have an anti-nociceptive effect at the central and/or spinal cord level [7]. However, there is evidence that this effect can be initiated by activation of peripheral opioid receptors [8]. The presence of peripheral opioid receptors is shown in immune cells and primary afferent neurons in animals [9].

It was speculated that administration of lower doses of opioids peripherally can provide more potent analgesia without central side effects such as respiratory depression, nausea, vomiting and pruritus [8]. Number of trials examined the peripheral analgesic effect of opioids as fentanyl in a large variety of surgical settings particularly arthroscopy, conduction nerve blocks, and local eye anesthesia [10–13].

To the best of our knowledge, this is the first study to compare different concentrations of fentanyl added to the local anesthetic mixture and their impact on the onset and duration of globe akinesia and analgesia after peribulbar regional eye block for cataract surgery.

2. Methodology

2.1. Patient population

A double blinded randomized controlled clinical trial of 60 cataractous patients of both sexes, in the age group 40–70 years, with ASA grade I, II and III, was conducted. Ethical committee approval and a written informed consent were obtained.

Complete ophthalmological examination, and ophthalmic ultrasound and biometry were done for all cases to exclude complicated vitreous hemorrhage, any associated disorders, and posterior staphyloma and also for measurement of the axial length.

The patients were divided randomly into 4 groups, each has 15 patients. Randomization was done by using a table of random numbers and sealed closed envelopes.

Patients with disturbed conscious level, uncontrolled hypertension, uncontrolled diabetes mellitus, recent myocardial infarction, having difficulty in communication e.g. mental retardation or deafness, history of abnormal bleeding, impaired orbital or periorbital sensation, history of allergy to local anesthetics or those with posterior staphyloma, axial length more than 28 mm and glaucoma were excluded.

2.2. Technique

An ampoule of hyaluronidase 1500 IU was dissolved by 1 ml of Lidocaine 2% and added to a vial of 49 ml of lidocaine 2% (hyaluronidase concentration is 30 IU/ml). 5 ml of this vial was taken and added to another 4 ml of lidocaine 2% (without hyaluronidase) and 1 ml normal saline with or without fentanyl was added to the above mixture.

No fentanyl was added to the local anesthetic mixture in Group 1 (Control Group), 10 μg fentanyl was added to the local anesthetic mixture in Group 2 (fentanyl concentration 1 μg/ml), 20 μg fentanyl was added to the local anesthetic mixture in Group 3 (fentanyl concentration 2 μg/ml) and 30 μg fentanyl was added to the local anesthetic mixture in Group 4 (fentanyl concentration 3 μg/ml).

All patients received the same volume of the local anesthetic mixture (7 ± 1 ml).

Before the block, a vein was cannulated, and ECG (Electro-cardiography), pulse oximetry and non invasive blood pressure were used as the standard monitors in all patients. Topical anesthesia to the infra orbital skin using EMLA cream will be applied at least 15 min before surgery. No sedative or hypnotic medications (midazolam, propofol or similar drugs) were given before or during the block.

Neither the anesthesiologist nor the patient was aware of the mixture chosen. One of the assistants was aware of the mixture chosen and had the code of the study.

A two-site-injection technique was used, under complete aseptic precautions. The first injection, transcutaneous inferolateral injection, was done using a standard 25 mm, 25 gauge needle with the gaze fixed straight ahead in the primary position, the injection site was identified by palpation of the infraorbital groove by the left index finger, at the same time, and the finger also was used to push the globe slightly and gently upwards. The needle was inserted to a depth of 20–25 mm, with the bevel of the needle cephalically directed toward the globe. The patients were then asked to look outward, inward, upward and downward to make sure that the globe was freely mobile and not transfixed by the needle. After negative aspiration, the local anesthetic mixture was injected (4–5 ml).

The second injection was done in the medial canthus using the same needle inserted in the blind pit between the caruncle and the medial canthus, and directed straight back parallel to the medial orbital wall with the bevel of the needle directed toward the globe. The needle was inserted to a depth of 15–20 mm. After negative aspiration, another volume of local anesthetic mixture (2–3 ml) was injected.

Immediately after injection, gentle digital massage was applied for 5–10 min to the closed eye to promote spread of the local anesthetic and to soften the globe.

Maximal lid opening, forceful lid closure and the extra-ocular muscle movements in the 4 cardinal directions were assessed before the block, and immediately after the block at 1 min, 3 min, 5 min and 10 min according to the scoring system that is shown in Table 1.

For assessment of lid akinesia, the patients were asked to open their eyelids (levator muscle) and then squeeze them together maximally (orbicularis muscle). Globe akinesia was assessed by examination of the movements of the extra-ocular muscles in all of the 4 main directions.

Table 1 Scoring system of levator and extraocular muscles akinesia [14].

Akinesia of extraocular muscles including the levator muscle
0 = 0–1 mm movement in 1 or 2 main directions
Or 0–4 mm movement in levator muscle
1 = 1 mm movement in more than 2 main directions or 2 mm movement in any main direction or more than 4 mm movement in levator muscle
2 = > than 2 mm movement in any main direction or 2 mm movement in 2 or more main direction
Akinesia of orbicularis muscle
0 = Complete akinesia
1 = Partial movement in either or both eyelid margins
2 = Normal movement in either or both eyelid margins

The block was considered to be satisfactory when loss of at least two movements of the 4 cardinal directions occurred. Failure of the block in certain patient leads to exclusion of that patient from the study who received general anesthesia. The assessment also was done intraoperatively and postoperatively by the same anesthesiologist, with the aid of the ophthalmologist. Both sides are compared for more accurate assessment of motor block. Arterial blood pressure, heart rate and arterial oxygen saturation (SpO_2) were checked before the block, then every 15 min during the entire procedure and every 30 min during the first two postoperative hours. Hypotension and bradycardia were defined as 20% or more decrease in the mean arterial blood pressure and heart rate, respectively, in relation to the preblock value.

Monitoring for the development of bradycardia or ventricular ectopics (oculo-cardiac reflex) was done and facilities were available for prompt management by immediate notification of the surgeon for temporary cessation of surgical stimulation until the heart rate increases and administration of IV atropine (10 μg/kg) if the condition persists.

Postoperative analgesia was assessed by using the numeric pain rating scale [15]every hour up to 6 h postoperatively as follows:

0 = no pain,
1, 2 and 3 = mild pain,
4, 5 and 6 = moderate pain,
7, 8 and 9 = severe pain,
10 = very severe pain or maximum pain imaginable.

If the numeric pain rating scale was more than 3, injection of Diclofenac 75 mg IM or Paracetamol 1000 mg IV was given. Enquiry was made about any expected adverse effects e.g. nausea, vomiting, dryness of the mouth, dizziness, confusion, diplopia or blindness.

Statistics were done by computer using Epi-info., software version 6.04. The results were reported as X (mean) ± SD (standard deviation) of the mean. Intergroup comparison of demographic data, axial length, onset and duration of akinesia and analgesia, pain scores, volume of local anesthetic injected and hemodynamic variables was made by one-way analysis of variance (ANOVA). For within-group comparison of data, paired Student's t-test was used. A value of $P \leqslant 0.05$ was considered statistically significant. The post study power was computed for duration of analgesia, lid and globe akinesia with 95% confidence interval.

3. Results

There was no statistically significant difference (Fig. 1) between the four groups (Table 2) in the onset or duration of both lid and globe akinesia as shown in Table 3, However, there was a significant difference between the control group (group 1) and the other groups as regards the duration of analgesia that was significantly prolonged in group 3 and group 4 as shown in Table 3.

We did not observe any side effects during the study related to the peribulbar block or any systemic side effects associated with the use of fentanyl in peribulbar block as sedation, confusion, hypotension, bradycardia, desaturation, nausea, vomiting or allergic reactions (see Table 4).

4. Discussion

Addition of Fentanyl to Lidocaine and Hyaluronidase for regional peribulbar block is a safe and effective method in improving postoperative analgesia in patients undergoing cataract surgery; however, this has no significant effect regarding the onset or duration of both lid and globe akinesia.

To the best of our knowledge only very few studies evaluated the addition of fentanyl to the local anesthetic mixtures used for regional peribulbar and retrobulbar blocks.

As regards the duration of analgesia, our study showed progressive prolongation of the duration of analgesia between the control group (no fentanyl was added to the local anesthetic mixture) and the other groups who received the local anesthetic mixture containing fentanyl and was significantly prolonged in groups 3 and 4 (in which 20 μg and 30 μg fentanyl were added to the local anesthetic mixture respectively).

Duration of analgesia was 100.00 ± 13.49, 103.66 ± 15.52, 116.00 ± 19.19, 144.00 ± 11.21 min in groups 1, 2, 3 and 4 respectively.

These results are in line with Mostafa et al. [12] who studied the effect of adding fentanyl 20 μg to mepivacaine, bupivacaine and hyaluronidase local anesthetic mixture in peribulbar block, compared to a control group that received the same local anesthetic mixture without fentanyl. They found that addition of fentanyl 20 μg to the local anesthetic mixture significantly prolonged the duration of globe analgesia. The first time to require analgesia was prolonged in the fentanyl group, in which 75% of patients required analgesia 3 h postoperative while in the control group, 30% required it in the first hour, 55% in the second hour and 15% in the third hour.

In the current study there was no statistically significant difference between the four groups regarding the onset and duration of lid and globe akinesia, which meant that the addition of fentanyl to the local anesthetic mixture did not fasten the onset nor prolonged the duration of the motor blockage of the lid or globe muscles.

On the contrary Mostafa et al. [12] showed that the addition of fentanyl 20 μg to the local anesthetic mixture in peribulbar block fastened the onset of the block as 80% of patients got lid akinesia at 3 min and no patients remained to 5 min while in the control group, 15% got complete lid akinesia at 5 min and 5% at 10 min.

Also the fentanyl group had a short onset of globe akinesia as 65% of patients got globe akinesia at 3 min, 30% at 5 min

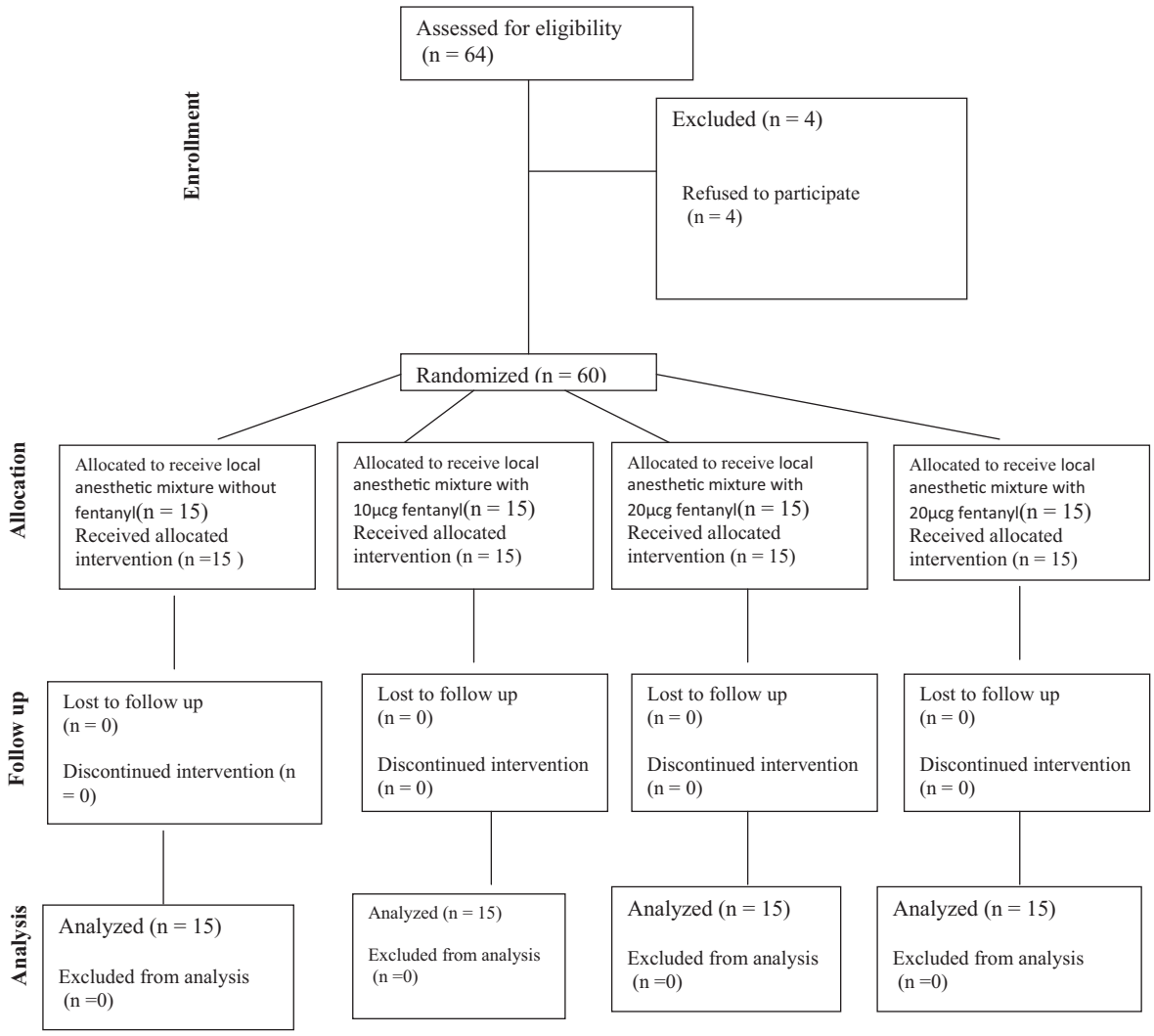

Figure 1 CONSORT diagram showing the flow of participants through each stage of a randomized trial.

Table 2 Data were presented as mean ± SD and percentage.

Variable	Group 1	Group 2	Group 3	Group 4
Age (years)	63.73 ± 9.30	59.20 ± 11.79	57.66 ± 10.23	57.20 ± 16.34
Male *n* (%)	7 (46.6)	7 (46.6)	10 (66.6)	11 (73.3)
Female *n* (%)	8 (53.4)	8 (53.4)	5 (33.4)	4 (26.7)
Weight (kg)	75.90 ± 9.30	73.11 ± 6.55	70.21 ± 7.10	80.45 ± 8.45
Volume (ml)	7.60 ± 1.01	7.90 ± 0.89	7.87 ± 0.55	7.45 ± 0.75
Duration of surgery (min)	65.50 ± 10.22	60.89 ± 10.55	70.75 ± 15.20	78.59 ± 14.27
AL (mm)	25.48 ± 1.52	24.70 ± 1.92	25.04 ± 1.24	24.71 ± 1.55

N (number), kg (kilogram), min (minute), ml (milliliter) and mm (millimeter).
Group 1 (control group), Group 2 (10 µg fentanyl was added to the local anesthetic mixture), Group 3 (20 µg fentanyl was added to the local anesthetic mixture), and Group 4 (30 µg fentanyl was added to the local anesthetic mixture).

and only 5% at 10 min while in the control group, 15% of patients got it at 3 min, 70% at 5 min and 15% at 10 min.

The fentanyl group also had longer duration of lid and globe akinesia than the control group. This difference may be attributed for giving 1 mg midazolam with 25 µg fentanyl intravenously together with application of topical anesthesia in the form of tetracaine eyedrops 0.5% in both groups in previous study.

However, in this aspect, our results are in line with Fahmy et al. [13] who evaluated the effect of adding fentanyl and/or clonidine to local anesthetic on prolongation of peribulbar block in cataract surgery in which 120 patients were enrolled in study, and they were classified randomly into four groups (group C = received 30 µcg clonidine, group F = received 20 µcg fentanyl, group F + C = received 15 µcg clonidine and 10 µcg fentanyl, and group S = received 2 ml saline in

Table 3 Duration of lid and globe akinesia and analgesia. Values are expressed as mean ± SD.

Variable	Group 1	Group 2	Group 3	Group 4
Onset of lid akinesia (min)	4.06 ± 0.96	3.00 ± 1.06	3.40 ± 0.98	3.40 ± 0.63
Onset of globe akinesia (min)	4.13 ± 0.99	3.73 ± 0.96	3.80 ± 0.94	3.40 ± 0.98
Duration of lid akinesia	79.00 ± 11.98	81.00 ± 12.42	84.00 ± 9.48	86.00 ± 6.86
Duration of globe akinesia (min)	86.33 ± 8.54	86.00 ± 14.41	87.00 ± 8.40	94.00 ± 10.55
Duration of analgesia (min)	100.00 ± 13.49	103.66 ± 15.52	116.00 ± 19.19 *	144.00 ± 11.21 *
NPR scale	6.40 ± 0.82	6.46 ± 1.35	7.06 ± 1.27	5.86 ± 2.06

Min (minute), NPR (numeric pain rating).
* $P \leqslant 0.05$.

Table 4 Duration of lid and globe akinesia and analgesia. Values are expressed as mean (95% confidence interval).

	Group 1 (n = 15)	Group 2 (n = 15)	Group 3 (n = 15)	Group 4 (n = 15)
Duration of lid akinesia	79.00 (72.94–85.06)	81.00 (74.71–87.29)	84.00 (79.2–88.8)	86.00 (82.53–89.47)
Duration of globe akinesia	86.33 (82.01–90.65)	86.00 (78.71–93.29)	87.00 (82.15–91.25)	94.00 (88.66–99.34)
Duration of analgesia	100.00 (93.17–106.83)	103.66 (95.81–111.51)	116.00 (106.29–125.71)	144.00 (138.33–149.67)

There was no overlap between group 4 and other groups and small overlap between groups 3 and 2.

addition to the LA mixture into the peribulbar block) and concluded that 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.

No side effects in the form of confusion, hypotension, bradycardia, desaturation, nausea, vomiting or allergic reactions were observed during the study related to the peribulbar block or associated with the use of fentanyl in peribulbar block.

5. Limitations

Very few randomized controlled trials were present which made it difficult for us to set comparison and to validate our results.

6. Conclusion

Adding Fentanyl at concentrations $\geqslant$ 2–3 μg/ml to the local anesthetic mixture (Lidocaine and Hyaluronidase) for regional peribulbar block provides safe and effective method in improving postoperative analgesia in patients undergoing cataract surgery; however, further randomized controlled studies enrolling larger number of patients are required to evaluate and validate these findings.

Conflict of interest

Professor Doctor Inas Kamel is an Author in this paper and honorary Chief of the Egyptian Journal of Anesthesia.

References

[1] Hamilton RC, Gimbel HV, Strunin L. Regional anaesthesia for 12,000 cataract extraction and intraocular lens implantation procedures. Can J Anaesth 1988;35:615–23.
[2] Ripart J et al. Peribulbar versus retrobulbar anesthesia for ophthalmic surgery: an anatomical comparison of extraconal and intraconal injections. Anesthesiology 2001;94:56–62.
[3] Gioia L et al. Peribulbar anesthesia with either 0.75% ropivacaine or a 2% lidocaine and 0.5% bupivacaine mixture for vitreoretinal surgery: a double-blinded study. Anesth Analg 1999;89:739–42.
[4] Yau G et al. The addition of fentanyl to epidural bupivacaine in first stage labour. Anaesth Intensive Care 1990;18:532–5.
[5] Davison JA. Features of a modern retrobulbar anesthetic injection for cataract surgery. J Cataract Refr Surg 1993;19:284–9.
[6] Alhassan MB, Kyari F, Ejere HO. Peribulbar versus retrobulbar anaesthesia for cataract surgery. Anesth Analg 2008;107:2089.
[7] Yaksh KL. Multiple opioid receptor systems in brain and spinal cord. Eur J Anaesth 1984;1:171–3.
[8] Stein C. Peripheral mechanisms of opioid analgesia. Anesth Analg 1993;76:182–91.
[9] Fields HL, Emson PC, Leigh BK, et al. Multiple opiate receptor sites on primary afferent fibres. Nature (London) 1980;284:351–3.
[10] Nishikawa K, Kanaya N, Nakayama M, et al. Fentanyl improves analgesia but prolongs the onset of axillary brachial plexus block by peripheral mechanism. Anesth Analg 2000;91:384–7.
[11] Tverskoy M, Braslavsky A, Mazor A, Ferman R, Kissin. The peripheral effect of fentanyl on postoperative pain. Anesth Analg 1998;87:1121–4.
[12] Mostafa A, Ismail E, Ahmed S, et al. Effect of fentanyl addition to local anaesthetic in peribulbar block. Ind J Anesth 2009;53:57–63.
[13] Fahmy Neveen G, Fahmy Adel M, Kamal Kareem Y. Effect of adding fentanyl and/or clonidine to local anesthetic on prolongation of peribulbar block in cataract surgery. Ain Shams J Anesth 2011, 4-3.
[14] Sarvela P, Johanna MD. 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.
[15] McCaffery M, Beebe A, et al. Pain: clinical manual for nursing practice. Louis (MO): Mosby St.; 1989.