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Original Article

Effect of Ultra-Low-Dose-Naloxone, added to fentanyl and lidocaine for peribulbar anesthesia

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ABSTRACT

Background: Use of fentanyl in local anesthesia, as adjuvant, is known to improve the block and prolong the duration of postoperative analgesia. This study aimed to evaluate the effect of addition of ultra-low-dose of naloxone to fentanyl and lidocaine for peribulbar anesthesia on the quality of the block and the duration of postoperative analgesia on patients undergoing globe cataract surgery.
Methods: 50 adult patients, of both genders, undergoing globe cataract surgery in the Department of Ophthalmology, GMC Jammu, were studied, in collaboration with the Department of Anesthesiology, during the period December 2014 to May 2015. The patients were divided into two groups of 25 each, comparable for the patient characteristics. Group 1 patients received 50 μg fentanyl and lidocaine 2% with hyaluronidase 15 IU/ml, while, Group 2 patients received 100 ηg naloxone, 50 μg fentanyl and lidocaine 2% with hyaluronidase 15 IU/ml.
Results: No significant difference in total injected volume, onset and best akinesia score or number needing supplemental injection. Time to first rescue analgesic was significantly longer in group 2 (7.05 ± 1.04) than group 1 (4.41 ± 0.39). VAS was quite low at 30, 60, 90 min and 2 or 3 h, but increased significantly after 4 hours in Group 1. A significant increase in the IOP, 2 min after injection of the local anesthetic.
Conclusion: Addition of ultra-low-dose naloxone to fentanyl and lidocaine for peribulbar anesthesia showed significant prolongation of the time to first request for analgesic without increasing the adverse effects.

Keywords: Globe Cataract Surgery, Naloxone, Fentanyl, Peribulbar Anesthesia

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INTRODUCTION

Use of fentanyl in local anesthesia, as adjuvant, is known to improve the block and prolong the duration of postoperative analgesia. It is used through intrathecal, and epidural routes, without increasing the side effects.[1] Fentanyl is also used as adjuvant to local anesthetic for peripheral nerve blocks, like: Intravenous regional anesthesia,[2] axillary brachial plexus block[3], or in intra-articular injection after knee arthroplasty.[4] Opioid receptors are expressed by central and peripheral neurons and can attenuate the excitability of primary afferent neurons, leading to anti-nociceptive effects.[5] Fentanyl as adjuvant to lidocaine, is considered safe, effective, but short-lived analgesia.[6] Studies have also discussed that ultra-low-dose (pg–ηg/kg) of naloxone combined with opioid agonists can improve their analgesic efficacy via blocking the excitatory opioid receptor pathway and enhancing opioid analgesia. [7,8]

Naloxone has not been used before with fentanyl as adjuvants to the local anesthetic in peribulbar anesthesia, in GMC Jammu, so, the aim of the present study was to evaluate the effect of addition of ultra-low-dose of naloxone to fentanyl and lidocaine for peribulbar anesthesia on the quality of the block and the duration of postoperative analgesia on patients undergoing globe cataract surgery.

METHODS

A randomized double blind prospective clinical-trial study was conducted in the Department of Ophthalmology in collaboration with the Department of Anesthesiology during the period November 2014 to April 2015 in GMC Jammu. 50 adult patients of both gender, undergoing globe cataract surgery, were selected, however patients with clotting abnormalities and on anticoagulant therapy, impaired mental status, patients with communication difficulties, uncontrolled movements or tremors e.g. Parkinsonism, inability to lie flat, one eyed patients, uncontrolled glaucoma, recent surgical procedure on the same eye, high myopia, with axial length ⩾26 mm as detected by ultrasonography, and allergy to hyaluronidase or local anesthetics, were excluded.

Ethical approval was duly obtained from Institutional Ethical Committee. The patients were divided into two groups: Group 1 (fentanyl group) and Group 2 (fentanyl-naloxone group) with 25 patients in each. The patients were randomized using a computer-generated random number and closed envelops to undergo peribulbar anesthesia. Group 1 patients received 50 μg fentanyl and lidocaine 2% with hyaluronidase 15 IU/ml, while, Group 2 patients received 100 ηg naloxone, 50 μg fentanyl and lidocaine 2% with hyaluronidase 15 IU/ml. The duration of analgesia, as indicated by the first time for rescue analgesic, measured from the time of onset to the first time of feeling of moderate or severe pain, was considered the primary end point.

Preoperatively, the patients were monitored for ECG, heart rate, pulseoximetry. Arterial blood pressure (ABP) was measured non-invasively every 5 min. Topical local anesthetic (benoxinate hydrochloride) was applied to the eye then, with the eye in the primary gaze position, a 25-gauge short bevel needle was inserted trans-conjunctivally at the junction between the medial two thirds and lateral third of the inferior orbital rim in a strictly posterior direction. The anesthetic mixture was injected after aspiration test and the injection was continued until sub-conjunctival edema and lid fullness appeared. Intermittent digital compression was applied to lower the intraocular pressure until sufficient motor block occurred.

The total volume of local anesthetic injected, time of onset of pain, first request for rescue analgesic and complications were duly recorded. If after 10 min, immobility was insufficient, 4 ml of the same solution was re-injected. Pain was assessed during and after surgery at 30, 60, 90 min, 2, 3 and 4 hours, postoperatively, using Visual Analogue Score (VAS) of 0 to 10 (0 = no pain and 10 = maximum pain).

The data were analyzed using SPSS 16.0 software and data was expressed as mean ± SD and analyzed using independent-t-test for comparison between the two groups. Gender and number of patients, who needed supplemental injection and complications, were expressed as percentage and $p < 0.05$ was considered statistically significant.

RESULTS

The two groups were comparable for the patient characteristics; age, gender, weight, and duration of surgery (Table 1). No significant difference between the two groups regarding the total injected volume, onset and best akinesia score, and also in the number of patients needing supplemental injection. However, the time to first rescue analgesic was significantly longer in group 2 (7.05 ± 1.04) than group 1 (4.41 ± 0.39). (Table 2)

The Intro-Ocular Pressure (IOP) increased significantly at 2 min post-injection compared to the pre-injection values in both groups. At the same time, there was a significant decrease in the IOP 10 min compared to 2 min post-injection in the two groups. (Table 3)

Table 1: Characteristics of studied groups

	Group 1 (n = 25)	Group 2 (n = 25)
Age (years)	55.41± 5.95	56.46 ± 5.73
Gender (male:female)	13:12	14:11
Weight (kg)	74.27 ± 6.88	72.20 ± 6.21
Duration of surgery (minutes)	50.44 ± 5.32	53.69 ± 4.67

Table 2: Quality of block

Group	Group 1 (n = 25)	Group 2 (n = 25)	p-value
Total injected volume (ml)	8.66 ± 1.30	9.12 ± 1.67	0.443
Onset (minutes)	9.50 ± 2.50	9.00 ± 2.50	0.409
Patients needed supplemental injection (%)	5 (20.0%)	3 (12.0%)	0.073
Time to first rescue analgesic (hours)	4.41 ± 0.39	7.05 ± 1.04	<0.001*

*p < 0.05 considered significant.

Table 3: Intra-ocular pressure

	Pre-injection	2 min post-injection	10 min post-injection	P value
Group 1 (n = 25)	10.26 ± 1.53	15.52 ± 1.77	12.41 ± 1.45	<0.001*
Group 2 (n = 25)	10.79 ± 1.48	15.19 ± 1.65	11.06 ± 1.10	<0.001*
p-value	0.336	0.209	0.114	

*p < 0.05 considered significant.

The Visual Analogue Score (VAS) was significantly lower at 30, 60, 90 min and 2 and 3 h, then increased at 4-hour and 6-hour time, postoperatively in both the groups. It heightened to the level, requiring analgesic after 4.41 ± 0.39 hours interval in Group 1, but was within mild levels for group 2 at 4 hours and 6 hours interval. The results were statistically significant. (p<0.001) (Figure 1).

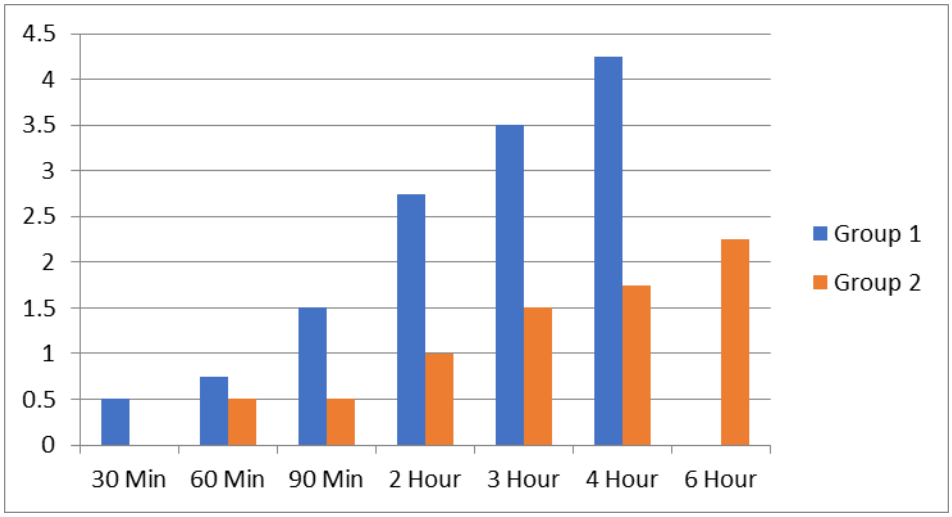

Figure 1: Intensity of pain (median range at various time- intervals)

As regards the complications,2 patients (8%) in group I, and 2 (8%) patients in group II had pain on injection. No diplopia, post-operative squint, globe perforation, or penetration occurred in any patient of the studied groups.

DISCUSSION

In the present study the VAS was significantly lower at 30, 60, 90 min and 2 and 3 h, then increased at 4-hour and 6-hour time, postoperatively in both the groups. It heightened to the moderate and extreme levels after 4 hours interval in Group 1, but was within mild levels for group 2 at 4 hours and 6 hours interval, showing significant prolongation of the time to first request for analgesic in the naloxone group. This was explained by Crain and Shen, who demonstrated that even an ultra-low-dose of naloxone (NLX) and naltroxone (NTX) have selective antagonistic effects on the excitatory opioid receptor functions, thus unmasking the inhibitory effects of morphine and other opioids.[9] It is further in agreement with the study of Movafegh et al.[10] who studied the effect of addition of ultra-low-dose of naloxone to lidocaine 1.5% with or without fentanyl in axillary brachial plexus block and they found that the ultra-low-dose of naloxone prolongs the time to first post-operative pain. Hamann et. al.[5] reported that the use of low dose (20 ηg) intrathecal naloxone, when added to intrathecal morphine (2 mg) lead to pain reduction of 60–80%, who can return to daily activities without further hospitalization. Similar to our study, a recent study by Hoda et al,[11] in 2014, have found that the time to first rescue analgesic was significantly longer in fentanyl-naloxone group (7.73 ± 0.98 Hours) than fentanyl group (4.30 ± 0.47 Hours).

In the present study, both groups saw a significant increase in the IOP, 2 min after injection of the local anesthetic, and became insignificant after 10 min. Also, there was a significant decrease in the IOP 10 min compared to 2 min post-injection. This indicates that, the intermittent digital compression was effective in reversing the increase in IOP after local anesthetic injection. Bowman et. al. has discussed that the transient increase in IOP was due to injection of local anesthetic in the limited orbital space, and then it decreased due to decrease of the external pressure on the globe as a result of relaxation of the extra-ocular muscles.[12]

CONCLUSION

In the present study, there were hardly any complications and adverse effects, hence we can conclude that, addition of ultra-low-dose naloxone to fentanyl and lidocaine for peribulbar anesthesia prolongs the duration of post-operative analgesia and decreases the analgesic requirement without increasing the adverse effects.

Conflict of interest: None
Ethical approval: Taken

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