Clinical Investigation

Comparative evaluation of ropivacaine and lignocaine with ropivacaine, lignocaine and clonidine combination during peribulbar anaesthesia for phacoemulsification cataract surgery

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ABSTRACT

Background: Peribulbar block is the most common type of local anaesthesia administered for cataract surgery, and continuous efforts are on to find a long-acting local anaesthetic (LA) drug with the safest pharmacological profile. **Objectives:** A double-blind, prospective and randomized study was carried out in our institute to compare the anaesthetic effects of ropivacaine with the combination of ropivacaine and clonidine in administration of peribulbar block for phacoemulsification cataract surgery. **Methods:** A total of 200 patients of both sexes aged 50–80 years of American Society of Anaesthesiologists grade I and II, scheduled for phacoemulsification cataract surgery under monitored anaesthesia care, were enrolled for the study. Patients were assigned into two groups of 100 each; ropivacaine group (R) and ropivacaine clonidine group (RC). Group R received 10 mL of LA solution containing 5 mL of 2% lignocaine, 5 mL of 0.75% ropivacaine and 100 units of hyaluronidase while group RC received 8 mL of a similar mixture with the addition of clonidine 1 μg/kg and saline to make a total volume of 10 mL. Heart rate (HR), mean arterial pressure (MAP), pulse oximetry (SpO_2), respiratory rate (RR), intraocular pressure (IOP), eye muscle movement scores and quality of peribulbar block were observed and recorded throughout the study period at regular intervals. At the end of the research project, the data was compiled systematically and was subjected to statistical analysis using the ANOVA test with *post hoc* significance for continuous variables and Chi-square test for qualitative data. Value of $P<0.05$ was considered significant and $P<0.0001$ as highly significant. **Results:** Demographic characteristics, SpO_2 and RR were comparable in both the groups. Mean HR and MAP were also comparable after a significant variation in the first 2–3 min ($P<0.05$). Onset and establishment of sensory and motor blocks were significantly earlier in the RC group ($P<0.05$). IOP decreased significantly during the first 6–7 min in the RC group after the administration of the peribulbar block. Duration of analgesia was prolonged in the RC group (6.5±2.1 h) as compared with the R group (4.2±1.8 h). The side-effect profile revealed a higher incidence of nausea, vomiting, headache and dizziness in Group R, while a considerably higher incidence of dry mouth was observed in Group RC. **Conclusions:** Addition of clonidine to ropivacaine not only decreases the total volume of LA to be used but also augments early onset and prolonged offset of sensory analgesia as well as provides smooth operating conditions with a good sedation level as well by providing a wider safety margin of LA.

Key words: Cataract, clonidine, peribulbar block, ropivacaine

INTRODUCTION

Life expectancy has increased over the last few years due to advanced medical diagnostic and therapeutic techniques. The trend is shifting towards a better quality of life by taking advantage of these medical

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advancements. As a result, an increasing number of patients are coming to the hospital for various therapeutic and diagnostic procedures. The increasing popularity of phacoemulsification day care cataract surgery has started drawing a huge proportion of the population to the ophthalmological outpatient department. Majority of these patients belong to the geriatric age group and are invariably suffering from various systemic diseases including hypertension, cardiac disease, diabetes, etc. Surgery in this population group is always challenging and is associated with various risks, whether it is performed under general anaesthesia or regional anaesthesia.[1,2]

Peribulbar block is the most common and safe technique employed worldwide for the operative treatment of cataract, specifically in the phacoemulsification procedure. Bupivacaine and lignocaine have been the traditional mainstay in administering peribulbar block. Ropivacaine is a relatively new amide local anaesthetic (LA) available in our country that is gaining popularity on account of its favorable cardiovascular and neurologic pharmacological profile.[3,4] Even though the safety margin of ropivacaine is quite high, a higher volume is used in achieving the desired anaesthetic effect due to a lower potency than bupivacaine while performing different surgeries thus raising the concerns of systemic toxicity.[5,6] The addition of clonidine, an α-2 agonist, as an adjuvant to the LA not only prolongs the duration of analgesia but also decreases the total volume of the LA to be used.[5-9]

Keeping the pharmacological profile of ropivacaine and clonidine in mind, we carried out a doubleblind randomized study in the Department of Ophthalmology and Anesthesiology of our institute for comparing the effects of ropivacaine with ropivacaine and clonidine in peribulbar block for phacoemulsification cataract surgery. The chief aims of this pharmacological comparison were to observe the effects on haemodynamic parameters, intraocular pressure (IOP) changes, duration of analgesia and a possible dose reduction of ropivacaine with the addition of clonidine.

METHODS

The permission from the institute's ethical committee was sought after submitting the protocol of research methodology to the appropriate authorities. Thereafter, 200 patients of both sexes, aged 50–70 years, of American Society of Anaesthesiologists (ASA) grade I and II, scheduled for phacoemulsification cataract surgery under monitored anaesthesia care were enrolled in the study. A written informed consent was obtained from all the patients after explaining to them the nature of the study. A thorough pre-anaesthetic evaluation was carried out and patients received a 150 mg tablet of ranitidine a night before and 2 h before on the morning of surgery with a sip of water. All the patients were given written instructions and were called directly from the home on the day of surgery in a fasting state.

Patients with cardiac disease, active ocular infection, single eye, receiving any anti-coagulants, anti-epileptic drugs, anti-psychotic medication, anti-glaucoma drugs and patients allergic to amide-type LAs were excluded from the study.

Patients were assigned to two groups, ropivacaine group (R) and ropivacaine clonidine group (RC), comprising of 100 patients each, and the randomization sequence were generated using a computerized randomization table kept centrally by a research staff nurse. Group R received 0.75% ropivacaine and 2% lignocaine in an equimixture ratio of 1:1 with a total volume of 10 mL, while group RC received a similar mixture of 8 mL but with the addition of 1 μg/kg of clonidine and saline to make a total volume of 10 mL. The study solutions were prepared by an ophthalmic technician who was given a written set of instructions and was unaware of the study design. All the patients and the researchers were masked to the treatment allocation group by wrapping the vial externally with aluminium foil.

The peribulbar block was performed by a senior resident of the ophthalmology department who had a vast experience in the regional blocks. The drug was injected at two places: At the medial 2/3rd and lateral 1/3rd of the lower eyelid and at the lateral 2/3rd and medial 1/3rd of the upper eyelid. To promote the spread of the LA solution and to decrease the IOP, orbital mechanical compression was exerted using a "pinky" rubber ball. In the pre-operative room, all the baseline parameters were observed and recorded, which included heart rate (HR), mean arterial pressure (MAP), pulse oximetry (SpO_2), respiratory rate (RR), IOP and eyelid movement scores, and these parameters were observed every minute and recorded at fixed time intervals as per protocol. IOP was measured using a Schiotz tonometer and ocular movement score was also evaluated during the same time period as IOP using a 3-point scoring system in all the four quadrants

(Grade 0=akinesia: Ocular movement <1 mm; Grade 1=moderately reduced ocular movements: >1 mm and <3 mm, and normal ocular movements, i.e. greater than 3 mm were assigned to Grade 2). Sedation scores were measured using a subjective grading scale (0=no sedation; 1=calm and composed; 2=opening eyes with verbal command; 3=opening eyes on gentle tactile stimulation; 4=opening eyes with vigorous shaking; 5=not arousable).

After the administration of peribulbar blocks, HR, MAP, RR and SpO_2 were observed and recorded at regular intervals of 5 min during the surgical period. Oxygen was also administered through bi-nasal prongs with an oxygen flow of 3 L/min. Quality of block was assessed both by the surgeon and by the patient. Post-operatively, patients were kept in a recovery ward and were observed for the return of ocular movements and the timing of the first rescue analgesia. All the patients were discharged on the next morning of surgery.

The sample size selected was much larger than that required for a 5-min difference in the time required to achieve adequate surgical anaesthesia, accepting a one-tailed α-error of 5% and a β-error of 5%. The selection of such a large sample was deliberate to eliminate any other confounding biases. At the end of the study, the data was compiled systematically and was subjected to statistical analysis using SPSS version 10.0 for windows and using ANOVA with *post hoc* significance for continuous variables and Chi-square test for qualitative data. Value of $P<0.05$ was considered significant and $P<0.0001$ as highly significant.

RESULTS

For all the patients who underwent cataract surgery, a proper record was maintained regarding the demographic characteristics, peribulbar block characteristics and haemodynamic and respiratory parameters. The following results were obtained, which were analyzed using statistical methods, and the value of $P<0.05$ was considered significant and $P<0.0001$ was considered highly significant.

The mean age in Group R (62.8±6.8 years) was very much comparable to the mean age in Group RC (61.2±7.1 years) ($P>0.05$). Duration of surgery in both the groups was comparable and non-significant on statistical analysis. To summate, all the demographic characteristics like age, weight, ASA grade, side of the eye operated and duration of surgery were comparable in both the groups, and were found to be statistically non-significant ($P>0.05$) [Table 1].

Akinesia was considered ideal when no movement of the eye could be seen in any of the directions and onset was significantly earlier in the RC group as compared with the R group [Figure 1] and complete ocular muscle blockade was also significantly early in the RC group as compared with the R group ($P<0.05$).

IOP increased transiently during the first 1–2 min after the administration of the block in both the groups, which came to the baseline value over the next 1 min, and the comparative change was not significant on statistical analysis [Figure 2]. Thereafter, the IOP started decreasing in both the groups, but it decreased significantly in the RC group ($P<0.05$) at 6–7 min. Thereafter, no significant difference could be recorded statistically in both the groups regarding the rate of fall of IOP. Overall, the IOP remained on the lower side in patients receiving clonidine as an adjuvant.

The onset of sensory anaesthesia was much earlier (3.8±1.6) in the RC group as compared with the R group (4.6±2.1), which was statistically significant

Table 1: Demographic profile of the patients who underwent phacoemulsification cataract surgery

Demographic characteristics	Group R (*n*=100)	Group RC (*n*=100)
Age (years) (mean±SD)	62.8±6.8	61.2±7.1
Gender M/F	69/31	62/38
Weight (kg) (mean±SD)	60.6±10.4	56.8±11.5
Side of eye R/L	44/56	61/39
ASA grade I/II	37/63	45/55
Duration of surgery in minutes (mean±SD)	24.4±4.6	22.6±5.3

ASA – American society of anaesthesiologists; R – Ropivacaine group; RC – Ropivacaine clonidine group

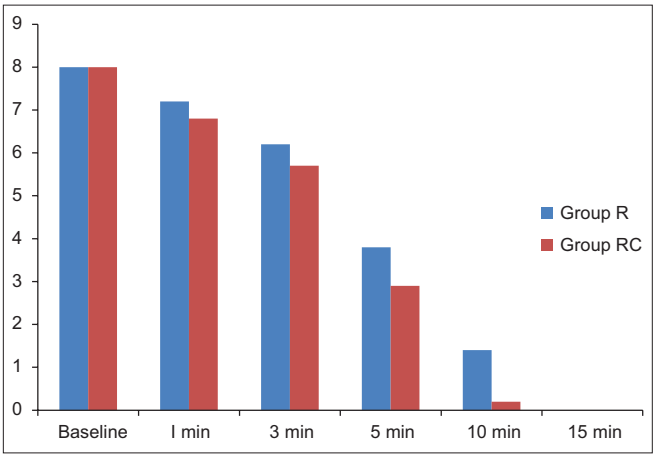

Figure 1: Mean akinesia scores in the groups R and RC at different time intervals pre-operatively

on comparison (P=0.012) [Table 2]. Similarly, the onset of motor blockade was significantly earlier in the RC group (4.1±2.3) than in the R group (7.4±2.7). The consumption of the total dose of LA solution was significantly lower in the RC group, but the block characteristics were comparable with the R group. The duration of first rescue analgesia was significantly prolonged in the RC group (6.5±2.1), and the post-operative period was perceived as smooth and pain-free by the majority of the RC group patients. None of the patients in either of the groups received additional administration of LA dose during the peri-operative period.

After the administration of peribulbar block, patients in both the groups had a transient increase in HR, which came to baseline within the next 1 min [Figure 3]. Thereafter, patients in the RC group had a sharper but a stable decline in HR as compared with patients in the Group R, which was statistically significant (P<0.05). The HR showed minimal variation in the RC group during the entire surgical period, but was significantly lower than the HR in the R group patients. MAP also projected a similar picture as mean HR. A significant statistical difference was observed at 15–20 min, and the difference remained the same during the rest of the surgical and recovery period.

Sedation scores during the peri-operative period were recorded at 5-min intervals, and were summated on an average basis to assign the grade for statistical analysis. Patients in the RC group had better sedation scores as compared with patients in the R group, as 48% and 27% of the patients in the RC group had highly significant sedation levels of grade 1 and 2, respectively, during the peri-operative period. On statistical analysis, all these corresponding values in both the groups turned out to be highly significant (P<0.0001).

The patient exhibited some remarkable statistical differences during the post-operative period [Table 3]. Six percent of the patients in the R group experienced nausea and 3% had episodes of vomiting as compared with those in the RC group, with a significant statistical incident of 3% and 1%, respectively. Headache was the chief complaint by 4% of the patients in the R group as compared with only 1% of the incidence in the RC group. Another interesting finding was the statistically significant and higher incidence of dry mouth in the patients of the RC group (17%) as compared with only 2% in the R group. None of the patients experienced pruritis and respiratory depression in our study.

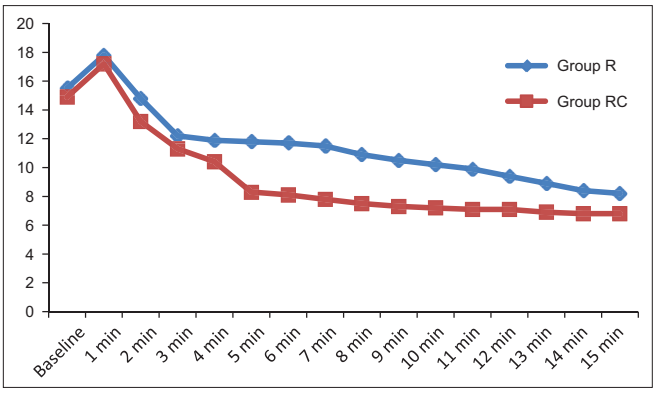

Figure 2: Comparative evaluation of intraocular pressure in the groups R and RC at different time intervals

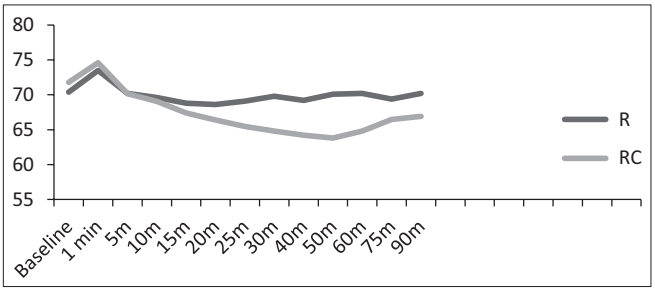

Figure 3: Comparison of heart rate in both the groups

Table 2: Comparison of peribulbar block characteristics in both the groups

Block characteristics	R	RC	*P*
Onset of sensory anaesthesia (min) (mean±SD)	4.6±2.1	3.8±1.6	0.012
Onset of motor blockade (min) (mean±SD)	7.4±2.7	4.1±2.3	0.006
Duration of analgesia (h)	4.2±1.6	6.5±2.1	0.004
Sedation during the peri-operative period			
Grade 0	88	17	<0.0001
Grade I	12	48	<0.0001
Grade II	1	27	<0.0001
Grade III	0	8	–

R – Ropivacaine group; RC – Ropivacaine clonidine group

Table 3: Incidence of side-effects in the groups R and RC

Side-effects	Group R	Group RC	*P*
Nausea	6	3	<0.05
Vomiting	3	1	<0.05
Headache	4	1	<0.05
Dizziness	5	3	>0.05
Dry mouth	2	17	<0.001

R – Ropivacaine group; RC – Ropivacaine clonidine group

DISCUSSION

Regional anaesthesia has gained massive popularity for day care phacoemulsification cataract surgery as it avoids complications and untoward events

associated with general anaesthesia.[10] The increasing preference for peribulbar blockade is focused not only at achieving adequate analgesia but also at obtaining satisfactory akinesia of the eye as well. The resulting decreased IOP provides ideal and smooth operating conditions for the surgeons. Ropivacaine was selected for administering peribulbar block on account of its favorable cardiac and neurologic profile as compared with bupivacaine.[3,4,11,12] Combination of 2% lignocaine in an equimixture of 1:1 was used in the present study on account of achieving an earlier onset with lignocaine and a possible prolonged duration of post-operative pain relief with ropivacaine.[10]

Similar observations to our study regarding block characteristics were recorded by few earlier studies while using 0.75% ropivacaine, 0.5% bupivacaine or 2% mepivacaine for different peripheral nerve blocks.[13-15] The higher concentration of ropivacaine (0.75%) may facilitate diffusion of LA molecules into peripheral nerves thus achieving an earlier nerve blockade as compared with bupivacaine 0.5%.

The motor blockade (akinesia) was achieved significantly earlier in the RC group at 10 min. Surprisingly, we observed a transient increase in the IOP in the first 1–2 min in both the groups, which could have been possibly due to the increase in intraorbital fluid volume with injection of LA causing increased orbital pressure. The increase in HR and MAP during the first 2 min after the peribulbar block can possibly be explained on the basis of pain during the administration of peribulbar block. At 3–4-min interval, IOP, HR and MAP returned to the baseline values, which can be possible due to relaxation of the extraocular muscle and, interestingly, these observations also coincided with the onset of sensory analgesia.

Ropivacaine is also reported to have a vasoconstrictive effect, which helps in lowering the IOP by decreasing the intraocular blood volume.[16] Clonidine is an α-2 agonist and augments the action of LA in regional blockades by interrupting the neural transmission of painful stimuli in Aδ and C fibres as well as augments the blockade of LA agents by increasing the conductance of K^+ ions in nerve fibres. It also exerts a vasoconstricting effect on smooth muscles, which results in a decreased absorption of the LA drug and, eventually, prolongs the duration of analgesia.[17,18] Clonidine is also known to decrease IOP, which was very much evident in the RC group from the 6th minute onwards after the administration of peribulbar block.[9,19]

Prolongation of motor blockade is a desirable feature that is preferred in phacoemulsification cataract surgery.[20] Although we achieved a satisfactory motor blockade in the R group also, the significant prolonged motor blockade achieved with addition of clonidine in the RC group can be of great help in the ophthalmic surgery of prolonged duration. The mild sedative effect of clonidine is an added advantage as the patients remained calm and composed during the entire surgical period and had better sedation scores than patients who were administered ropivacaine alone.

The usage of supplementary anaesthesia during ophthalmic surgeries is reported to be as high as 54%.[21] The addition of clonidine as an adjuvant to LA not only enhanced the duration of analgesia but also allowed the use of a lower volume of ropivacaine in the RC group thus reducing the concerns for potential systemic toxicity due to a larger volume of LA.[6]

Recovery from the motor blockade was highly comparable in both the groups and did not show any significant difference except during the initial earlier onset in the RC group. In spite of the addition of clonidine, motor block was not affected much in duration and did not match the duration of sensory analgesia. The pulse oximetry observation and the respiratory rate also did not show any significant change during the entire study period in both the groups.

The side-effect profile in both the groups showed some remarkable differences. The plain LA injection of ropivacaine was associated with a higher incidence of headache, dizziness, nausea and vomiting as compared with addition of clonidine with LA. The addition of clonidine was also not free of side-effects, as a mildly discomforting dry mouth was experienced by 17% of the patients. The decreased incidence of side-effects in the RC group can possibly be explained on the basis of a lower dose usage of ropivacaine as well as the addition of clonidine.

CONCLUSIONS

Peribulbar is the safest form of local anaesthesia in phacoemulsification cataract surgery, and ropivacaine

is considered to be a good LA agent available that has got a favorable side-effect profile. The addition of clonidine not only decreases the total volume of LA to be used for the blockade but also augments early onset and a prolonged offset of the duration of sensory analgesia as well as provides smooth operating conditions with a milder level of sedation. We conclude that addition of clonidine in peribulbar block can widen the safety margin of the LA.

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