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# Efficacy and safety of Sodium Bicarbonate, Magnesium Sulfate, and Hyaluronidase as Additives to Peribulbar Anesthesia in Vitreoretinal Surgeries: A Randomized Double-Blind Comparative Study

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**KEYWORDS**

Peribulbar block, Vitreoretinal surgery, Hyaluronidase, Sodium bicarbonate, Magnesium sulfate, Akinesia, Anesthesia..

**ABSTRACT**

**Background**: The peribulbar block represents the gold standard for vitreoretinal surgery in adults. However, a delayed start of globe akinesia and corneal anesthesia, a brief duration of analgesia, and a frequent requirement for block replacement restrict the utilization of local anesthetic drug mixes for peribulbar anesthesia. The use of adjuvants can improve the effectiveness of local anesthetic.

**Objective:** To evaluate the safety and efficacy of adding hyaluronidase, sodium bicarbonate, and magnesium sulfate to the local anesthetic mixture for peribulbar anesthesia during vitreoretinal surgery.

**Methods:** This randomized, double-blind, parallel-group clinical trial enrolled 75 patients scheduled for vitreoretinal surgery. Eligible patients were randomized to one of three groups of 25 patients each. All patients received a peribulbar local anesthetic injection in addition to 1 mL of hyaluronidase, 1 mL of sodium bicarbonate 8.4%, and 75 mg of magnesium sulfate in the hyaluronidase, bicarbonate, and magnesium groups, respectively.

**Results:** At 5 minutes after block, complete globe akinesia was evident in all patients in the hyaluronidase and magnesium groups (100% each), which was significantly higher than in the bicarbonate group (56.0%). The onset of eyelid akinesia was rapid in both the hyaluronidase and magnesium groups, occurring with almost equal frequency 3 minutes after block (52% and 56%, respectively; P=0.777). In contrast, only 20% of the bicarbonate group had lid akinesia at 3 minutes, a significantly lower incidence than that observed in the hyaluronidase (P=0.018) and magnesium (P=0.009) groups. The onset of globe anesthesia was rapid in the hyaluronidase group, followed by the magnesium group and then the bicarbonate group, with a statistically significant difference. At the 5-minute post-block time point, intraocular pressure was significantly lower in the hyaluronidase and magnesium groups than in the bicarbonate group (18.4±2.0, 18.6±2.0, and 20.5±2.3, respectively).

**Conclusion:** Hyaluronidase and magnesium sulfate were more effective than sodium bicarbonate. The efficacy of hyaluronidase and magnesium sulfate in improving the onset of lid and globe akinesia and lowering intraocular pressure was comparable. However, the use of sodium bicarbonate as an adjuvant was associated with a high incidence of complications.
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## INTRODUCTION

Vitreoretinal surgeries are among the most common operations performed globally. Because of the length of the procedure, the need for a stationary field, and the strength of the surgical stimulation, vitreoretinal surgery was traditionally performed mostly under general anesthesia. Because it is safe, affordable, and offers efficient ocular anesthetic, there has been a noticeable movement over the past 20 years toward vitreoretinal procedures being carried out under carefully managed local anesthesia (LA) [(1)].

One of the most frequently utilized forms of LA is the peribulbar block. However, this method has some disadvantages, including delayed onset of action, increased intraocular pressure (IOP), inadequate analgesia, and a shift in the primary eye gaze [(2)]. Consequently, various additive medications to LA have been studied to increase the efficacy of local anesthetics (LAs), including the acceleration of the onset of anesthesia, the prolongation of the anesthetic effect, and the reduction of postoperative pain [(3)].

Adjuvant substances, including hyaluronidase [(4)], adrenaline [(5)], sodium bicarbonate [(6)], clonidine [(7)], magnesium sulfate [(8)], corticosteroids [(9)], and neuromuscular blocking agents [(10)], have been used in this context. The adjuvant use of hyaluronidase with LA is a well-established practice in ophthalmic surgeries. It facilitates greater dispersion of LAs around the orbit and the use of lower volumes, thereby enhancing the efficacy and safety of the procedure [(11)].

Some investigations have shown that adding sodium bicarbonate to LAs provides safe and beneficial advantages in vitrectomy surgery in terms of early onset and full ocular anesthesia, as well as IOP reduction [(12)]. Magnesium sulfate has been studied in combination with LA solutions in a variety of regional anesthesia procedures. Its usage has been reported to shorten blocking onset time while improving anesthetic quality and duration [(13)]. However, few studies have examined magnesium sulfate as an adjunct to the LAs for a peribulbar block [(8, 14)].

The reported success of the abovementioned LAs additives is limited [(14)], and several negative side effects, including allergic responses, bradycardia, sedation, dry mouth, and systemic neuromuscular blockade, were also linked to their usage [(15)]. Currently, no ideal adjuvant for the peribulbar block has been reported. So, research is ongoing to identify the most efficient and safe LA adjuvant that also offers cost-effective advantages [(14)].

Therefore, this study aimed to compare the efficacy and safety of hyaluronidase, sodium bicarbonate, and magnesium sulfate as an additive to standard local anesthetics mixture for peribulbar anesthesia in vitreoretinal surgery.

## METHODS

### Study design, setting, and date

This randomized, double-blinded, parallel-group clinical trial was carried out at the Anesthesia Department of the Research Institute of Ophthalmology (RIO) Hospital, Egypt, from April 2024 to October 2024

### Ethical considerations

The Research Ethics Committee of Egypt's Research Institute of Ophthalmology (RIO-REC) granted ethical authorization for this study. Each patient gave informed written consent. Each participant was assigned a code number to maintain data confidentiality.

### Sample size

A priori sample size calculation was carried out using G*power 3.1.9.2 software. Based on previous studies of **Arafa and El-Sayed [(12)] and Sherif et al. [(16)]** who used sodium bicarbonate and magnesium sulfate as adjuvants to peribular block and the assumption that hyaluronidase gives

similar results to sodium bicarbonate in reducing IOP, the sample size was calculated according to the significant differences between the mean values of the IOP in the magnesium sulfate (32.1±5.4), sodium bicarbonate (18.65±1.57) and hyaluronidase (17.32±2.43) groups in one-way ANOVA test, with α=0.05, power of 80%, and an effect size of 0.4. So, a sample size of 22 eyes per group was required that was increased to 25 eyes per group to allow for a 15% dropout rate.

**Eligibility criteria**

The study comprised male and female patients aged 18 to 70 years old who had an American Society of Anesthesiologists (ASA) physical status I or II and were scheduled for vitreoretinal surgery under peribulbar block anesthesia. We eliminated ASA III or IV patients who were on anticoagulant medication, as well as those with coagulopathy, an allergy to the LA drugs utilized, severe tremors or agitations, or ocular deformity. Uncooperative patients and those who refused to participate in the study were also removed.

**Randomization, allocation concealment, and blinding**

The simple randomization process was conducted using a computer-based random number generator, and the sealed, opaque envelopes were employed to maintain the concealment of the allocation. To ensure blinding, an anesthesiologist prepared the drug solutions, labeled them, and transferred them to another anesthesiologist, who was responsible for the peribulbar block and data collection while blinded to the contents of the syringes.

**Study procedures**

Before surgery, all patients fasted for six hours. The patient was connected to a multichannel monitor in the operating room, which recorded the baseline ECG, heart rate, systolic and diastolic blood pressure, and oxygen saturation. A 20 or 22G cannula was placed. With a nasal cannula that supplies oxygen at a rate of three liters per minute, the patient was put in a supine posture.

The anesthetic peribulbar technique was performed after sterilization of the physician’s hands and patient eye with Benoxinata HCL 0.4% topical anesthetic drops. Depending on the patient group, a 26 G, 13 mm short bevel needle attached to a syringe holding the adjuvant was used to administer the injection. After a negative aspiration, the needle was inserted twice, and three to five milliliters of local anesthetic with adjuvant were administered at each site. After this injection, the eye was gently compressed intermittently for five to ten minutes.

**Interventions**

Seventy-five eligible patients were randomly allocated into three groups: The hyaluronidase group (Group A, N=25) received a local anesthetic mixture of 4ml of lidocaine 2% and 4ml of bupivacaine 0.5% with 1ml of hyaluronidase (1500 IU in 30 ml of lidocaine). The sodium bicarbonate group (Group B, N=25) received a local anesthetic mixture of 4ml of lidocaine 2% and 4ml of bupivacaine 0.5% with 1ml sodium bicarbonate 8.4% (1 ml of sodium bicarbonate 8.4% diluted in 10 ml of normal saline). The Magnesium sulfate group (Group C, N=25) received a local anesthetic mixture of 4 ml of lidocaine 2% and 4 ml of bupivacaine 0.5% with 75 mg of magnesium sulfate (one ampoule of magnesium sulfate 100 mg/ml)

**Outcomes**

The primary outcome was the onset of globe akinesia, which was assessed using a 3-point scale recorded at 1-, 3-, and 5-minute post-block. The scale was as follows: 0 = complete akinesia, 1 = limited akinesia, and 2 = normal movement. The onset of lid akinesia and globe anesthesia was assessed at 1-, 3-, and 5- minute post-block, with the outcome classified as either "occurred" or "not occurred." Intraocular pressure was measured at baseline and 1-, 3-, and 5- minute post-injection of local anesthesia using a Schiotz tonometer.

The secondary outcomes included the necessity for analgesics at 1-, 2-, and 4-hours postoperatively. The motor block was evaluated clinically at 1-, 2-, and 4-hours postoperatively, with a score of either "vanished motor block" (0) or "sustained motor block" (1). Immediately following the block, patient and surgeon satisfaction was assessed and classified as either satisfied or not. Vital data, including heart rate, systolic and diastolic blood pressure, and oxygen saturation, were recorded at 5-minute intervals during the operation and analyzed at 15-minute intervals. All patients were watched for any negative occurrences, and if any occurred, they were noted.

**Statistical analysis**

Using IBM SPSS Statistics for Windows, version 27.0, data were analyzed. We used the Shapiro-Wilk test to evaluate the distribution of numerical data. Normally distributed variables were displayed as mean± SD, and One-Way ANOVA was used to assess for differences among the three groups. Following significant results, post hoc analysis was conducted using the Games-Howell test. Frequencies and percentages were used to summarize categorical variables, and $X^2$ tests (independence, Pearson's Chi-square, or Fisher-Freeman-Halton Exact Test, as appropriate) were used to test the relationships between the variables. Post hoc tests were used to identify pairwise differences when the results were significant. When the P-value was less than 0.05, it was deemed statistically significant.

**RESULTS**

This randomized clinical trial enrolled 75 patients scheduled for vitreoretinal surgery under peribulbar block anesthesia. Patients were randomly assigned to receive either hyaluronidase (n=25), sodium bicarbonate (n=25), or magnesium sulfate (n=25). All patients received the assigned interventions, completed follow-up at the designated time intervals, and were included in the final analysis **(Figure 1).**

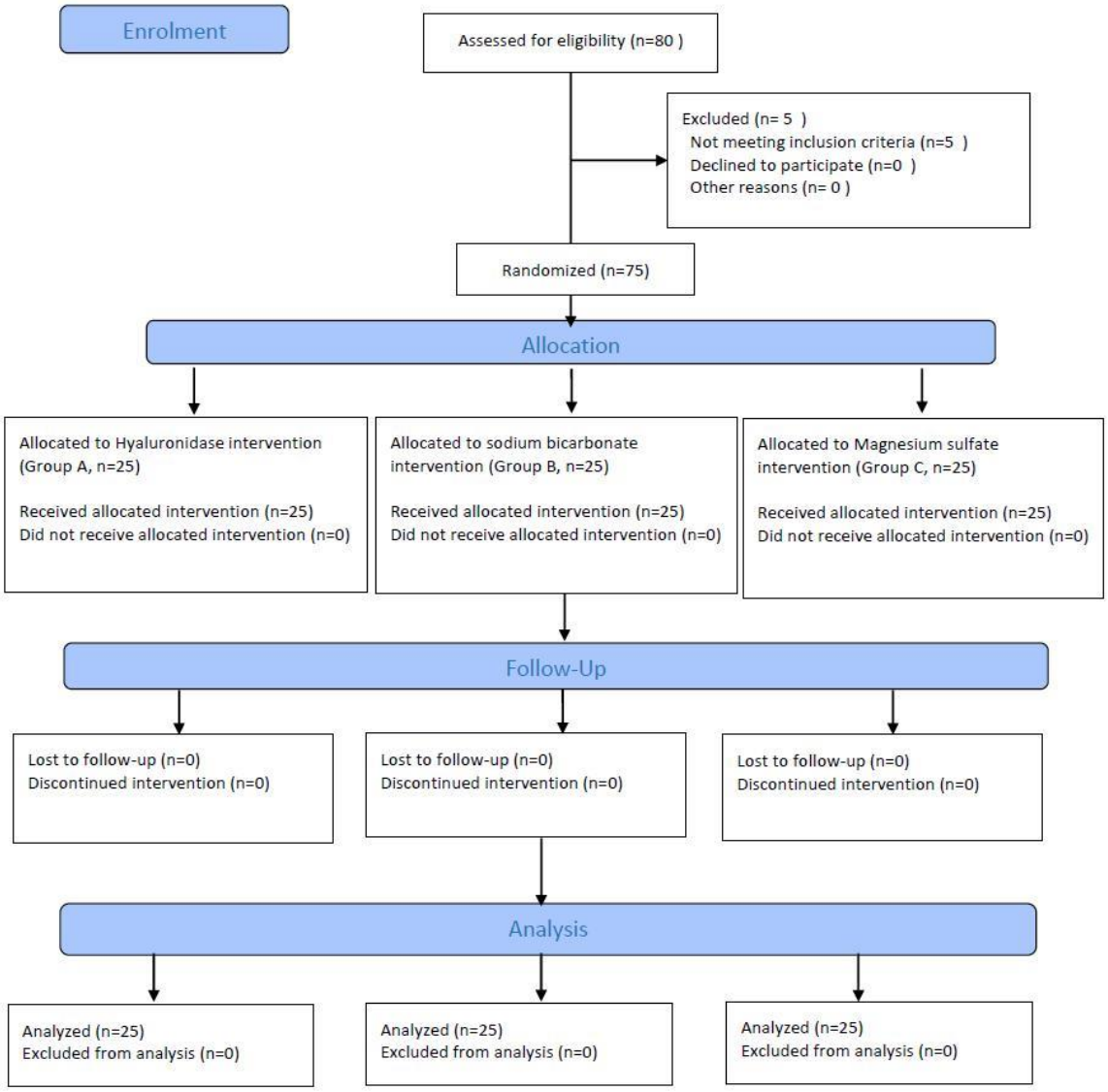


**Figure (1): CONSORT flow chart of the trial**

The three patient groups exhibited comparable distributions of age, sex, and ASA status, with no statistically significant differences (all P>0.05) **(Table 1).**

**Table (1): Basic characteristics of the studied three groups**

| | | **Group A Hyaluronidase (N=25)** | | **Group B Bicarbonate (N=25)** | | **Group C Magnesium sulfate (N=25)** | | **P-Value** |
|---|---|---|---|---|---|---|---|---|
| **Age, years** | Mean± SD | 54.1±10.7 | | 53.3±13.5 | | 57.0±8.6 | | 0.471 |
| **Sex, N %** | Female | 13 | 52.0% | 14 | 56.0% | 14 | 56.0% | 0.948 |
| | Male | 12 | 48.0% | 11 | 44.0% | 11 | 44.0% | |
| **ASA, N %** | I | 6 | 24.0% | 5 | 20.0% | 8 | 32.0% | 0.846 |
| | II | 16 | 64.0% | 17 | 68.0% | 13 | 52.0% | |
| | III | 3 | 12.0% | 3 | 12.0% | 4 | 16.0% | |

ASA: American Society of Anesthesiologists, SD: standard deviation

The onset of globe anesthesia was rapid in the hyaluronidase group, followed by the magnesium group, and then the bicarbonate group, with a statistically significant difference. At 1-minute following the peribulbar block, more than half (52.0%) of the hyaluronidase group showed globe anesthesia compared to 20.0% in the magnesium group (P=0.001). Conversely, no cases in the bicarbonate group demonstrated anesthesia. At 3 min, the frequency of globe anesthesia increased in both the hyaluronidase and magnesium groups (96.0% each), resulting in a significantly higher prevalence compared to the bicarbonate group (20%). At 5 min, all groups showed comparable rates, with no observed significant differences **(Table 2).**

The onset of lid akinesia was rapid in both the hyaluronidase and magnesium groups, occurring at nearly equal frequencies at 3-minute after the block (52% and 56%, respectively; P=0.777). In contrast, only 20% of the bicarbonate group exhibited lid akinesia at 3 min, a significantly lower incidence than that observed in the hyaluronidase (P=0.018) and magnesium (P=0.009). Notably, none of the groups demonstrated lid akinesia at 1 min, while all patients in the three groups exhibited lid akinesia at the 5-minute mark **(Table 2).**

Globe akinesia was absent in all three groups at 1 min, and limited with comparable distribution in all three groups at 3 min. At 5-minute after the block, complete globe akinesia was evident in all patients belonging to the hyaluronidase and magnesium groups (100% each) which was significantly higher than in the bicarbonate group (56.0%), with a P-value of less than 0.001 for both comparisons **(Table 2).**

**Table (2): Comparison between the studied groups regarding onset of globe anesthesia and akinesia**

| | | **Group A Hyaluronidase (N=25)** | | **Group B Bicarbonate (N=25)** | | **Group C Magnesium Sulfate (N=25)** | | **P-Value** | **Post hoc test** |
|---|---|---|---|---|---|---|---|---|---|
| **Globe anesthesia (1min)** | No | 12 | 48.0% | 25 | 100.0% | 20 | 80.0% | <0.001* | P1<0.001*<br>P2=0.001*<br>P3=0.050 |
| | Yes | 13 | 52.0% | 0 | 0.0% | 5 | 20.0% | | |
| **Globe anesthesia (3min)** | No | 1 | 4.0% | 20 | 80.0% | 1 | 4.0% | <0.001* | P1<0.001*<br>P2=0.999<br>P3<0.001* |
| | Yes | 24 | 96.0% | 5 | 20.0% | 24 | 96.0% | | |
| **Globe anesthesia (5min)** | No | 1 | 4.0% | 0 | 0.0% | 1 | 4.0% | 0.999 | NA |
| | Yes | 24 | 96.0% | 25 | 100.0% | 24 | 96.0% | | |
| **Lid akinesia (1min)** | No | 25 | 100.0% | 25 | 100.0% | 25 | 100.0% | NA | NA |
| **Lid akinesia (3min)** | No | 12 | 48.0% | 20 | 80.0% | 11 | 44.0% | 0.019* | P1=0.018*<br>P2=0.777<br>P3= 0.009* |
| | Yes | 13 | 52.0% | 5 | 20.0% | 14 | 56.0% | | |
| **Lid akinesia (5min)** | Yes | 25 | 100.0% | 25 | 100.0% | 25 | 100.0% | NA | NA |
| **Globe akinesia (1min)** | 2 | 25 | 100.0% | 25 | 100.0% | 25 | 100.0% | NA | NA |
| **Globe akinesia (3min)** | 1 | 17 | 68.0% | 14 | 56.0% | 17 | 68.0% | 0.594 | NA |
| | 2 | 8 | 32.0% | 11 | 44.0% | 8 | 32.0% | | |
| **Globe akinesia (5min)** | 0 | 25 | 100.0% | 14 | 56.0% | 25 | 100.0% | <0.001* | P1<0.001*<br>P2 NA<br>P3<0.001* |
| | 1 | 0 | 0.0% | 11 | 44.0% | 0 | 0.0% | | |

*Significant at p<0.05, P1: Group A versus Group B, P2: Group A versus Group C, P3: Group B versus Group C, NA: not applicable. Scores of globe akinesia: 0; complete akinesia, 1; limited akinesia, 2; normal movement.

At the 5-minute time point after the block, the IOP was significantly lower in the hyaluronidase and magnesium groups than in the bicarbonate group (18.4±2.0, 18.6±2.0, and 20.5 ±2.3, respectively), with no significant differences between the hyaluronidase and magnesium groups (P=0.935). Otherwise, the IOP readings demonstrated no significant differences between the three groups at the baseline, 1, and 3-minute time points **(Table 3).**

**Table (3): Evaluation of intraocular pressure at different time points in the three studied groups**

| IOP | Group A Hyaluronidase (N=25) | | Group B Bicarbonate (N=25) | | Group C Magnesium Sulfate (N=25) | | P-Value | Post hoc test |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | | |
| **Baseline** | 17.0 | 2.4 | 17.2 | 2.5 | 17.6 | 2.9 | 0.740 | NA |
| **At 1min** | 22.1 | 2.1 | 22.4 | 2.2 | 22.2 | 2.6 | 0.856 | NA |
| **At 3min** | 19.7 | 2.0 | 21.1 | 2.3 | 20.1 | 2.0 | 0.060 | NA |
| **At 5min** | 18.4 | 2.0 | 20.5 | 2.3 | 18.6 | 2.0 | 0.001* | P1=0.003*P2 =0.935 P3=0.008* |

*Significant at p<0.05, IOP: intraocular pressure, SD: standard deviation, P1: Group A versus Group B, P2: Group A versus Group C, P3: Group B versus Group C, NA: not applicable

A follow-up conducted at 1, 2, and 4 hours post-operatively demonstrated that the duration of motor block was significantly prolonged in the magnesium group when compared to the hyaluronidase and bicarbonate groups. At 1 h, all patients in the three groups exhibited sustained motor block. At 2 h, the sustained motor block was observed in an equal proportion of patients in the hyaluronidase and magnesium groups (76%) compared to 24.0% in the bicarbonate group. At 4 h, the motor block was sustained in 10 patients (40.0%) in the magnesium group, while it had completely vanished in the hyaluronidase and bicarbonate groups, with significant differences (p < 0.001 each). Furthermore, the requirement for analgesics at 2 h following the procedure was significantly higher in the bicarbonate group (76.0%) than in the hyaluronidase and magnesium groups (24% each). At 4 h, the need for analgesics was significantly lower in the magnesium group (76.0%) relative to the hyaluronidase and bicarbonate group (100%) **(Table 4).**

**Table (4): Postoperative assessment of globe motor block and analgesia at different time points in the three studied groups**

| | | Group A Hyaluronidase (N=25) | | Group B Bicarbonate (N=25) | | Group C Magnesium Sulfate (N=25) | | P-Value | Post hoc test |
|---|---|---|---|---|---|---|---|---|---|
| Motor block at 1h | 1 | 25 | 100.0% | 25 | 100.0% | 25 | 100.0% | NA | NA |
| Motor block at 2h | 0 | 6 | 24.0% | 19 | 76.0% | 6 | 24.0% | <0.001* | P1<0.001* P2 =1.00 P3<0.001* |
| | 1 | 19 | 76.0% | 6 | 24.0% | 19 | 76.0% | | |
| Motor block at 4h | 0 | 25 | 100.0% | 25 | 100.0% | 15 | 60.0% | <0.001* | P1 NA P2<0.001* P3<0.001* |
| | 1 | 0 | 0.0% | 0 | 0.0% | 10 | 40.0% | | |
| Need for | No | 25 | 100.0% | 25 | 100.0% | 25 | 100.0% | NA | NA |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| analgesia at 1h | | | | | | | | | |
| Need for analgesia at 2h | Yes | 6 | 24.0% | 19 | 76.0% | 6 | 24.0% | <0.001* | P1 <0.001* P2=1.00 P3<0.001* |
| | No | 19 | 76.0% | 6 | 24.0% | 19 | 76.0% | | |
| Need for analgesia at 4h | Yes | 25 | 100.0% | 25 | 100.0% | 19 | 76.0% | 0.002* | P1 NA P2=0.022* P3=0.010* |
| | No | 0 | 0.0% | 0 | 0.0% | 6 | 24.0% | | |

*Significant at p<0.05, P1: Group A versus Group B, P2: Group A versus Group C, P3: Group B versus Group C, NA: not applicable, motor block score 0: vanished, motor block score 1: sustained

Concerning patient and surgeon satisfaction, the hyaluronidase and magnesium groups exhibited comparable outcomes (100% and 92%, respectively), which were significantly higher than those observed in the bicarbonate group (28.0%). The incidence of complications was significantly higher in the bicarbonate group than in the hyaluronidase and magnesium groups. No complications were observed in the hyaluronidase group. Two patients in the magnesium group exhibited subconjunctival hemorrhage. Monitoring of the bicarbonate group revealed the occurrence of increased intraocular pressure in six patients (24%), periocular ecchymosis in five patients (20%), pain and discomfort in four patients (16%), and eyelid swelling in three patients (12%) **(Table 5).**

**Table (5): Comparison of patients and surgeon satisfaction and incidence of complications between the three studied groups**

| | | **Group A Hyaluronidase (N=25)** | | **Group B Bicarbonate (N=25)** | | **Group C Magnesium Sulfate (N=25)** | | **P-Value** | **Post hoc test** |
|---|---|---|---|---|---|---|---|---|---|
| **Patient satisfaction** | Not satisfied | 0 | 0.0% | 18 | 72.0% | 2 | 8.0% | <0.001* | P1<0.001* P2=0.490 P3 <0.001* |
| | Satisfied | 25 | 100.0% | 7 | 28.0% | 23 | 92.0% | | |
| **Surgeon satisfaction** | Not satisfied | 0 | 0.0% | 18 | 72.0% | 2 | 8.0% | <0.001* | P1<0.001* P2=0.490 P3 <0.001* |
| | Satisfied | 25 | 100.0% | 7 | 28.0% | 23 | 92.0% | | |
| **Complications** | No | 25 | 100.0% | 7 | 28.0% | 23 | 92.0% | <0.001* | P1<0.001* P2=0.490 P3 <0.001* |
| | Increased IOP | 0 | 0.0% | 6 | 24.0% | 0 | 0.0% | | |
| | Periocular ecchymosis | 0 | 0.0% | 5 | 20.0% | 0 | 0.0% | | |
| | Pain and discomfort | 0 | 0.0% | 4 | 16.0% | 0 | 0.0% | | |
| | Eye lid swelling | 0 | 0.0% | 3 | 12.0% | 0 | 0.0% | | |
| | Subcongunctival hemorrhage | 0 | 0.0% | 0 | 0.0% | 2 | 8.0% | | |

*Significant at p<0.05, IOP: intraocular pressure, P1: Group A versus Group B, P2: Group A versus Group C, P3: Group B versus Group C

The results of intraoperative hemodynamic monitoring indicated a reduced mean heart rate in groups A and C when compared to group B at both 75 and 90 minutes. The mean heart rates for groups A, B, and C were 53.7, 60.9, 57.8, and 53.7, 74.3, and 57.8, respectively. At the 90-minute mark, the mean systolic blood pressure was significantly lower in groups A and C (126.4 and 126.6, respectively) compared to group B (138.3). Similarly, at the 90-minute mark, the mean diastolic blood pressure was significantly lower in groups A and C (69.3 and 69.7, respectively) compared to

group B (77.4). Oxygen saturation was comparable among the three groups at all-time points **(Figures 2, 3, 4, and 5).**

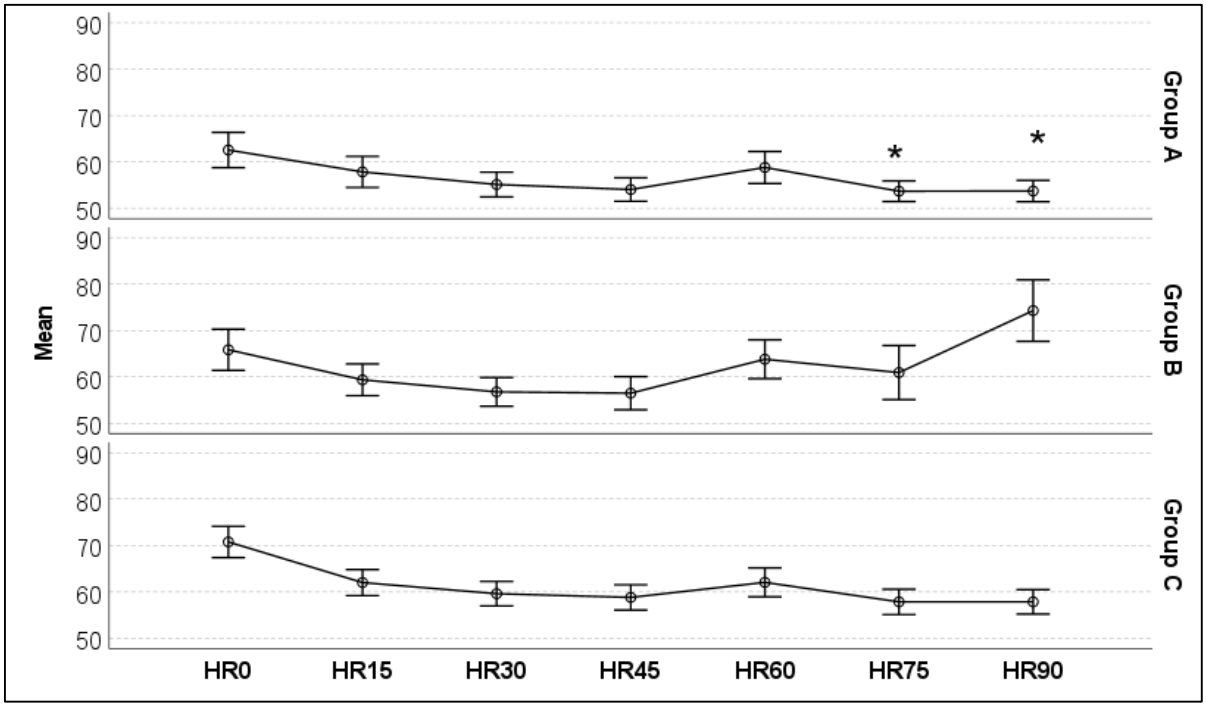


**Figure (2): The means and 95% confidence interval (error bars) of the heart rate over 15-minutes interval in the three studied groups. * indicates significant differences between group A vs group B and group B vs group C at 75 and 90 minutes.**

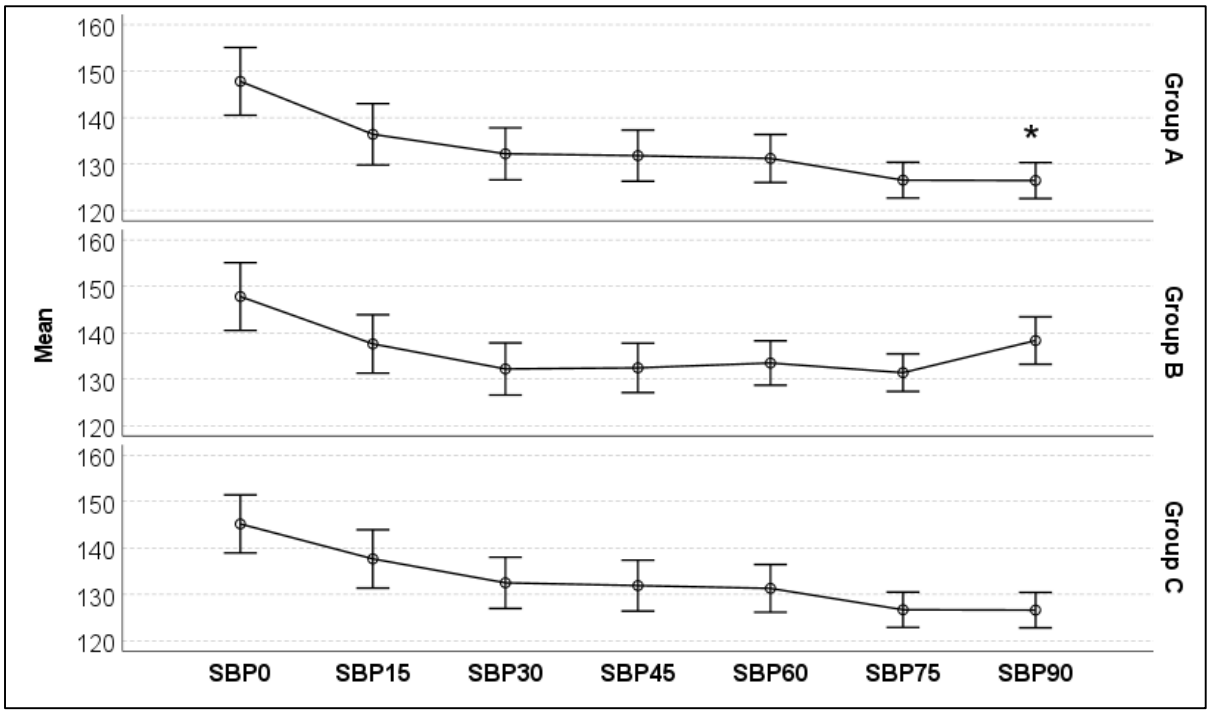


**Figure (3): The means and 95% confidence interval (error bars) of systolic blood pressure over 15-minutes interval in the three studied groups. * indicates significant difference between group A vs group B and group B vs group C at 90 minutes.**

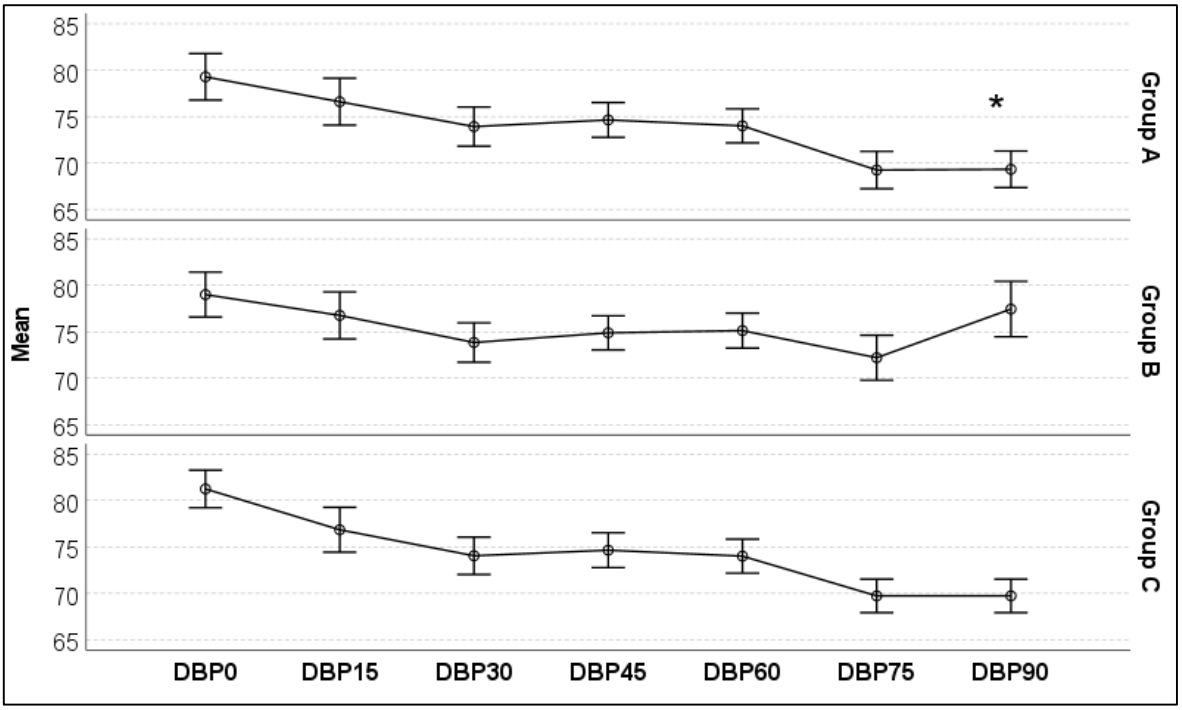


**Figure (4): The means and 95% confidence interval (error bars) of the diastolic blood pressure over 15-minutes interval in the three studied groups. * indicates significant differences between group A vs group B and group B vs group C at 90 minutes.**

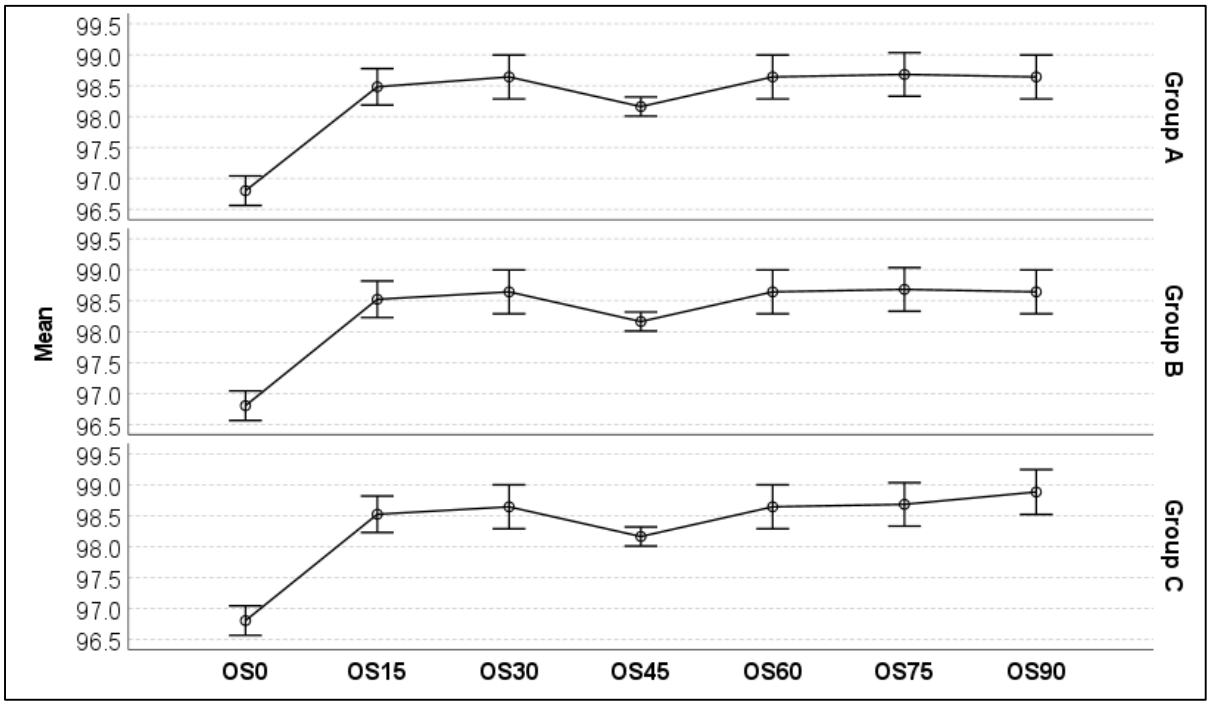


**Figure (5): The means and 95% confidence interval (error bars) of the oxygen saturation over 15-minutes interval in the three studied groups.**

## DISCUSSION

The peribulbar block is the gold standard for vitreoretinal surgery in adults. However, traditional local anesthetic drug mixtures for peribulbar anesthesia have significant drawbacks. They frequently lead to a brief period of analgesia, a delayed start of globe akinesia and corneal

anesthesia, and a frequent requirement for block replacement. The use of adjuvants can improve the effectiveness of local anesthetic [17].

The ongoing research into the comparative effectiveness and safety of hyaluronidase and magnesium versus bicarbonate has the potential to provide further insights and support for their use in clinical practice. Therefore, this study compared the motor and sensory anesthetic efficacy in terms of onset and duration of akinesia and anesthesia, IOP when adding hyaluronidase, sodium bicarbonate, or magnesium sulfate to the peribulbar anesthesia in vitreoretinal surgeries.

Magnesium and hyaluronidase both improved the block properties with relation to the development of globe and lid akinesia. In comparison to the bicarbonate additive, the time to commencement of lid akinesia and entire globe akinesia was considerably shortened when either hyaluronidase or magnesium was added to LAs. In addition, hyaluronidase considerably shortened the globe anesthesia onset time in contrast to the magnesium and bicarbonate groups. Five minutes after injection, these results lead to a shorter surgical delay and better operating circumstances.

It is known that the enzyme hyaluronidase aids in the breakdown of hyaluronic acid, which is an extracellular matrix component. When used in conjunction with LAs, it has been demonstrated to enhance the spread and absorption of the anesthetic, thereby facilitating a quicker and more effective muscle paralysis with a faster onset of akinesia in the eyelids and globe during ocular procedures [18]. Nevertheless, hyaluronidase has certain disadvantages, including pain at the injection site, expense, a shorter half-life, and limited accessibility. Furthermore, magnesium sulfate has the potential to act as a neuromuscular blocker when administered in specific doses. It has been demonstrated that this agent can facilitate the reduction of neuromuscular transmission [19]. Magnesium sulfate's anesthetic and analgesic properties might be explained by its activity as a physiological calcium channel blocker and noncompetitive antagonist of N-methyl-D-aspartate receptors [13], bicarbonate is frequently employed to alkalinize LAs, which can enhance their efficacy and speed of onset. However, its impact on akinesia is typically more gradual compared to hyaluronidase and magnesium, as it primarily modifies the pH of the anesthetic rather than directly influencing neuromuscular transmission [20].

In accordance with these findings, **Sodani et al.** [20] have reported better effects of hyaluronidase than bicarbonate on globe anesthesia and akinesia in patients who underwent cataract surgery. Additionally, **Mohankumar and Rajan** [18] shown that hyaluronidase works well as an adjuvant in sub-tenon, peribulbar, and retrobulbar anesthesia during cataract surgery. They came to the conclusion that hyaluronidase produces analgesia and anesthesia quickly while using less amounts of anesthetic drugs, which results in fewer adverse effects. Alternatively, an earlier study concluded that pH adjustment using bicarbonate adjuvant reduces the onset time of peribulbar anesthesia [21].

Prior research on vitreoretinal surgery has described the quick onset of anesthesia and globe and lid akinesia that occurs when magnesium sulfate is added to peribulbar block LAs [8, 14], and in adult patients undergoing peribulbar block for elective eye surgery [15]. In line with our findings, **Jimoh et al.** [22] conducted a comparative analysis of the effects of magnesium sulfate and hyaluronidase as adjuvants in peribulbar anesthesia for cataract surgery. Their results indicated an earlier onset and longer duration of akinesia among the magnesium sulfate group than in the hyaluronidase, but the postoperative pain scores were comparable. **Narang et al.** [23] also observed an enhanced onset of sensory and motor block with the addition of magnesium sulfate as an adjunct to lignocaine in cases of upper limb surgery under intravenous anesthesia. Nevertheless, **Hamawy and Bestarous** [24] found that there was no advantage to the onset of the block when magnesium sulfate was added to the local anesthetic in peribulbar anesthesia for cataract surgery.

In this study, the magnesium group showed a significantly prolonged duration of motor block compared to the hyaluronidase and bicarbonate groups. Also, the addition of magnesium was associated with a significantly prolonged duration of sensory block reflected as prolonged post-

operative analgesia rather than the hyaluronidase and bicarbonate groups. The bicarbonate group showed the shortest duration of anesthesia, with the highest requirement for analgesics at 2 and 4 hours postoperatively. This agrees with **Sherif et al.** [25] who found that giving 100 mg of magnesium sulfate along with the LAs helped to extend the block's duration and resulted in low median VAS ratings following strabismus surgery. **Mogahed et al.** [26] also noted that using magnesium sulfate in the peribulbar block for cataract surgery reduced the need for postoperative analgesics and lengthened the duration of akinesia, and a similar finding has recently reported by **Gaddaf Eldam et al.** [27]. Supporting evidence of anesthetic effects of magnesium sulfate was previously documented when magnesium was given to prilocaine for axillary nerve block [28], as well as the epidural block [29].

Regarding the IOP, the addition of either hyaluronidase (18.4±2.0) or magnesium (18.6±2.0) to the local anesthetic mixture resulted in a significantly lower mean IOP at 5 minutes after injection compared to the bicarbonate group (20.5 ±2.3). **Mohamed et al.** [30] found a similar significant decrease in IOP readings in the magnesium group compared to a control group in the peribulbar block for ophthalmic surgeries. In contrast, **Arafa and El-Sayed** [12] recorded that sodium bicarbonate was effective in lowering IOP after performing peribulbar block for vitreoretinal Surgeries.

The incidence of complications was significantly higher in the bicarbonate group than in the hyaluronidase and magnesium groups. No adverse effects or complications related to the technique or the hyaluronidase drug were observed. Two patients in the magnesium group developed subconjunctival hemorrhage. Monitoring of the bicarbonate group revealed various complications including the occurrence of increased IOP in six patients (24%), periocular ecchymosis in five patients (20%), pain and discomfort in four patients (16%), and eyelid swelling in three patients (12%).

The patients were hemodynamically stable throughout the procedure except for a significant slight decline in the heart rate at 75- and 90-minute in the hyaluronidase and magnesium groups than in the bicarbonate group, with concomitant slight differences in the systolic and diastolic blood pressures at 90 min. Furthermore, both surgeon and patients satisfactions were the same (100%) for the hyaluronidase and magnesium adjuvants. However, patient and surgeon satisfactions were significantly lower in the bicarbonate group (28.0%).

## CONCLUSIONS

The present study demonstrated the superior efficacy and safety of hyaluronidase and magnesium sulfate as adjuvants to LAs in peribulbar blocks for vitreoretinal surgery in adults when compared with sodium bicarbonate. The efficacy of hyaluronidase and magnesium sulfate in enhancing the onset of lid and globe akinesia, as well as in reducing IOP, was comparable. Furthermore, both agents were associated with the complete satisfaction of the surgeon and the patients. However, the use of hyaluronidase demonstrated a more rapid onset of anesthesia than magnesium sulfate and was associated with the absence of complications. Magnesium sulfate, on the other hand, exhibited a prolonged duration of sensory block, with prolonged post-operative analgesia rather than the hyaluronidase. The sodium bicarbonate adjuvant was not only less effective than hyaluronidase and magnesium sulfate, but it was associated with a high incidence of complications.

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