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Role of Remifentanil in prevention increase of intraocular pressure after endotracheal intubation under Succinylcholine chloride

Haider Abbass Hassen[1]✉, **Iyad Abbas Salman**[2], **Mohammed Kassim A. Hassan**[1]

[1]Anaesthetist, Department of Intensive Care, Al-Imamain medical city, Baghdad, Iraq
[2]Consultant Anaesthetist, Medical College, University of Baghdad, Iraq

✉**Corresponding author**
Anaesthetist, Department of Intensive Care, Al-Imamain medical city,
Baghdad, Iraq;
Email: hayder.adnan2010@gmail.com

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ABSTRACT

Objective: To evaluate the role of remifentanil in decreasing intraocular pressure (IOP) after endotracheal (ET) intubation under the effect of Succinylcholine (rapid sequence induction). *Methods*: a prospective, randomized double-blinded clinical trial, done on 36 patients who had elective surgery in the ophthalmology department, we had studied the changes in IOP after succinylcholine injection and tracheal intubation 3 different times, by dividing patients into two groups, group R who takes Remifentanil 1 µg/kg and propofol 2 mg/kg induction, and group C who received 5 ml normal saline with propofol 2mg/kg induction. *Results*: Patients respond well, IOP had been decreased significantly in the remifentanil group, p-value between the two groups were less than 0.05. *Conclusions*: Remifentanil has a significant effect on decreasing IOP in rapid sequence induction and ET intubation.

Keywords: Remifentanil, intraocular pressure, IOP, glaucoma, endotracheal intubation, Succinylcholine, rapid sequence induction, vitreous humor

1. INTRODUCTION

Intraocular pressure (IOP) represents the pressure of the fluids in the eyes. The eye globe is a relatively non-compliant compartment; the volume of internal structures is fixed except for aqueous fluid and choroidal blood volume. The pressure of between 11 and 21 mmHg is considered normal. Many factors may increase intraocular pressure in anesthesia. Changes in choroidal blood volume can increase IOP. Hypercapnia causes choroidal congestion, coughing, straining or vomiting can increase IOP to 30 to 40 mm Hg. ET intubation can cause a similar increase. These increases are transient and are relatively innocuous in a closed eye but in an open eye, such as after a traumatic injury or during cataract surgery, these increases can lead to loss of intraocular contents, hemorrhage, and

permanent vision loss (Leonardi *et al.*, 2004). These increases in IOP during anesthetic procedures may be prevented by avoiding the hypertensive response to intubation and extubation. This may be achieved by using a laryngeal mask, propofol, clonidine, β-blockers, or high-dose opioids, by extubation under deep sedation or by covering ETT with lidocaine gel (Kohli *et al.*, 2007, Saeed and Fawzi, 2020). The pharmacokinetic profile of remifentanil is well suited to obtunding the rise in IOP which accompanies laryngoscopy and ET intubation. Remifentanil 1 μg/kg, administered over 30 s before induction with propofol and succinylcholine, attenuates the rise in IOP after intubation to levels less than those recorded before induction. In our study, we evaluate the role of remifentanil in decreasing IOP after succinylcholine injection and tracheal intubation (rapid sequence induction).

2. PATIENTS AND METHODS

Study design and setting

A double-blind randomized study, which was carried out in Ghazi al-Hariri Surgical Specialties Hospital, in the Ophthalmology department between October 2018 and August 2019. The study included 36 patients with ASA class 1and 2, undergoing elective eye surgery. Patients were allocated randomly to two groups:

Group R received anesthetic induction with propofol 2 mg/kg slow injection over 30 seconds, remifentanil 1 μg/kg, and Succinylcholine 1.5 mg/kg

Group C (control) received anesthetic induction propofol 2 mg/kg slow injection over 30 seconds, 5 ml normal saline, and Succinylcholine 1.5 mg/kg

Both groups maintained on Isoflourane and mechanical ventilation-controlled pressure mode 15 cm H_2O. Six patients were dropped from the study due to receiving hemodynamically active drugs which effect study measurements. The anesthetist performing induction and the ophthalmology surgeon were unaware of which study had been administered.

Inclusion criteria

Age from 12 to 66 years, and ASA class 1or 2

Exclusion criteria

Increased IOP or glaucoma, allergy to study drugs, patient refusal, emergency eye surgery, chronic opioids use eye surgery in the last 6 months, and anticipated difficult airway.

Study drugs

Remifentanil 1 μg/kg for R group patients, and normal saline for control group C. These drugs were prepared and aspirated in two 5 ml syringes which were labeled with different codes referred to as study drugs, not revealed until completing measuring. All patients are premeditated with midazolam 1-2 mg 10 minutes before induction, and tetracaine 0.5% local drops to the non-operated eye to facilitate IOP measuring.

Study parameters

Continuous monitoring during the time of eye surgery for mean arterial pressure (MAP), heart rate (HR), SPO_2, and ECG. In the study, SCHIØTZ tonometer had been used to measure IOP for the non-operated eye by another ophthalmologist. The measurement data was recorded 3 times:

After induction with propofol and study drug (before Succinylcholine injection)

Immediately after intubation (1 min after Succinylcholine injection)

During maintenance (5 min after Succinylcholine injection)

Statistical analysis

All analyses carried out using SPSS version 21.1, ANOVA (repeated measures analysis of variance ANOVA) used to assess the change in various parameters during the study period, p-value was considered to be significant if <0.05.

3. RESULTS

The two group's measurement data were compared to each other, by p-value was 0.0001 between two groups in all times recorded for IOP, the p-value was 0.0003 between two groups in all times recorded for MAP, and the p-value was 0.0002 between two groups in all times recorded for HR (figures 1 – 3).

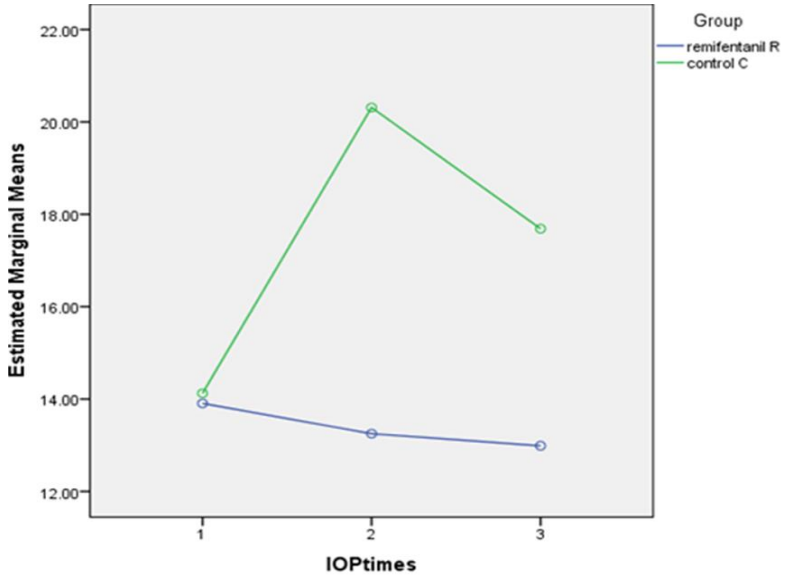

Figure 1 For comparison between 2 groups in IOP 3 times using ANOVA; (1) Before Succinylcholine injection, (2) 1 minute after Succinylcholine injection, and (3) 5 minutes after Succinylcholine injection

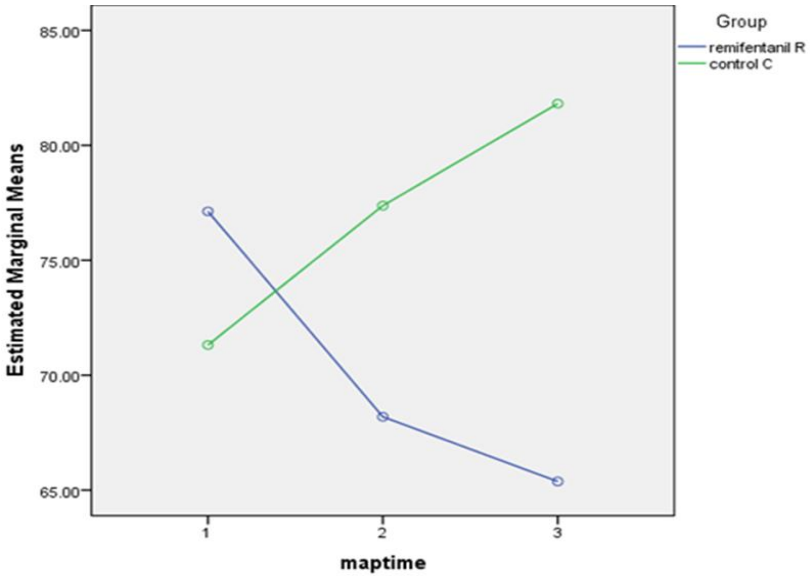

Figure 2 for comparison between 2 groups in MAP 3 times using ANOVA; (1) Before Succinylcholine injection, (2) 1 minute after Succinylcholine injection, and (3) 5 minutes after Succinylcholine injection

4. DISCUSSION

We observe from the above diagrams: (1) Group C (without remifentanil), IOP overshoot especially 1 minute after Succinylcholine injection then start to decrease, even after 5 min from Succinylcholine IOP still high, but in group R remifentanil show a significant effect by inhibition of the increase in IOP, and gradually decrease IOP, keeping a steady level. (2) Regarding MAP and HR in group C there was an impressive increase, due stress response to intubation, but in group R remifentanil obtund sympathetic reflexes so MAP and HR decrease from basal readings, increasing risk for hypotension and bradycardia, but still at an acceptable level. This study showed that remifentanil 1 µg/kg IV, as part of a rapid-sequence induction technique with propofol 2 mg/kg IV and Succinylcholine 1.5 mg/kg, provided good intubating conditions, decreasing IOP, and abolishing the hemodynamic stress response and overshooting in IOP associated with direct laryngoscopy and intubation.

Until the present day, the use of succinylcholine is controversial in patients with penetrating eye injuries. The increase in IOP after administration of succinylcholine may depend on the timing and dose of the drug, the special tonic response of the Felderstruktur fibers in the extraocular muscles, or a direct effect of succinylcholine on choroidal blood volume or aqueous humor formation. The risk of vitreous expulsion as a result of increased IOP needs to be balanced against the risk of aspiration of gastric contents (Alexander *et al.*, 1998). So remifentanil should be administered with an induction agent during rapid sequence induction to facilitate

smooth laryngoscopy and intubation of the trachea, in addition to preventing the hypertensive response and increase in IOP. The mechanisms underlying the prevention increasing of IOP include decreased choroidal blood volume due to decreased blood pressure, decreased ocular wall tension due to relaxation of the EOM via depression of the central diencephalic centers, decreased formation of aqueous humor, and the facilitation of aqueous outflow (Chang *et al.*, 2020).

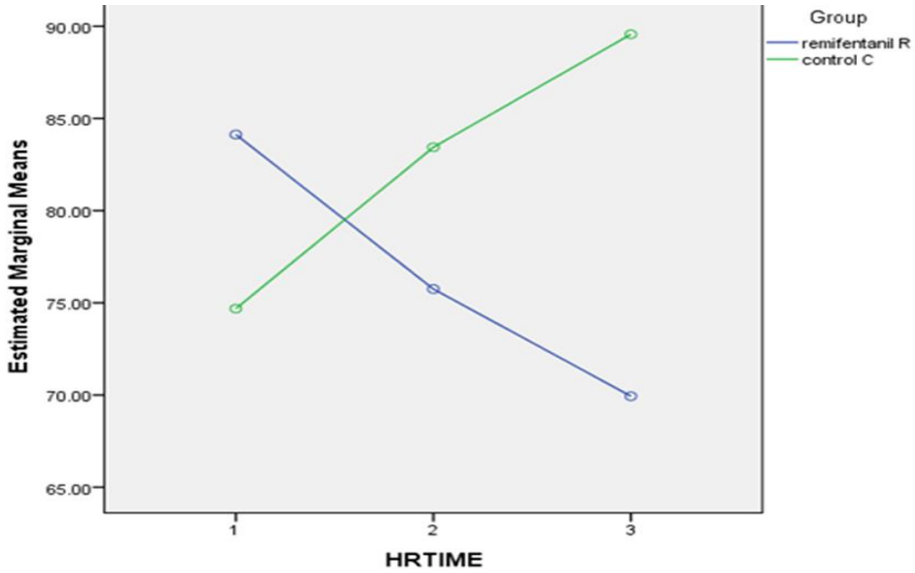

Figure 3 for comparison between 2 groups in HR 3 times using ANOVA; (1) Before Succinylcholine injection, (2) 1 minute after Succinylcholine injection, and (3) 5 minutes after Succinylcholine injection

Sung YF et al. 1994 have studied the effect of remifentanil on IOP by a dose of 0.05 µg/kg/min. Six minutes later, intermittent boluses of remifentanil 0.5 µg/kg were given for 15–20 s at 1-min intervals, until patients were adequately sedated (eyes closed, but rousable to command). IOP at the time of adequate sedation was not different from that at baseline, but IOP at 6 min and before the surgery decreased by 1.5- and 1.2-mm Hg, respectively. The decrease was statistically significant but was considered by Sung et al. not to be clinically meaningful (Artru, 1999). High dose remifentanil infusion and repeated bolus doses>1µg/kg increasing the risk of hypotension and bradycardia. In our study we used remifentanil as a part of GA induction by propofol and muscle relaxant (Succinylcholine), adverse effects of high dose remifentanil avoided, and clinically in our study, there was a significant decrease in IOP. Most anesthetic drugs decrease IOP in some way and it seems that using remifentanil alone is not beneficial in preventing IOP increasing (Chang *et al.*, 2020).

Alexander et al. 1998 had studied the role of remifentanil in preventing overshooting IOP after Succinylcholine injection and tracheal intubation studying changes in intraocular pressure (IOP) in 30 patients after succinylcholine and tracheal intubation following administration of propofol 2mg/kg and either remifentanil 1µ/kg(group R) or saline (groups). IOP was measured before induction, before administration of succinylcholine and the study drug, before intubation and for every 1 min after intubation for 5 min. There was a significant decrease in IOP after administration of the study drug ($P<0.006$). Our study results match this study by using the same dose (Alexander *et al.*, 1998).

Ng et al. published an article about the superiority of 1 µg/kg remifentanil over 2 µg/kg fentanyl in decreasing IOP after administration of succinylcholine and intubation. Remifentanil obtunded the increase in IOP more than fentanyl after succinylcholine and intubation. This study is consistent with our study in showing the effect of remifentanil on decreasing IOP in rapid sequence induction (Ng *et al.*, 2000). Sator-Katzenschlager et al. have compared the effects of remifentanil and fentanyl on intraocular pressure during the maintenance and recovery of anesthesia in patients undergoing elective non-ophthalmic surgery. The study showed a significant decrease in IOP by using 1µg/kg bolus dose of remifentanil in propofol/vecuronium maintained anesthesia. This study showed the efficacy of remifentanil as shown in our study with the deference of using maintenance 0.25-0.5 µg/kg/min remifentanil and measuring of IOP throughout the operation and after extubation but it shows the same results of our study after intubation (Sator-Katzenschlager *et al.*, 2004).

Kenan kaygusuz et al. 2007 investigated the effect of different doses of remifentanil show that IOP rise associated with the laryngoscopy and endotracheal intubation can be prevented by alfentanil 20 µg /kg or remifentanil 1 µg /kg without any hemodynamic instability, but remifentanil 0.5 µg /kg used with the same purpose may not be sufficient. This study is consistent with our study in using remifentanil 1 µg/kg to prevent increasing of IOP during and after intubation (Kaygusuz *et al.*, 2007). Sherine F.

Hanna et al. 2008 had published a study to evaluate the effect of propofol (2 mg/kg)/remifentanil (4 µg/kg) on intraocular pressure (IOP) when used for rapid-sequence induction without a muscle relaxant. The high dose of remifentanil provided intubation condition comparable to those of succinylcholine but at the expense of causing a significant decrease in MAP by up to 31%. This is partially consistent with our study in showing the effect of remifentanil in decreasing IOP and differs in that we provide optimal intubation condition by Succinylcholine and to avoid the adverse effect of high remifentanil dose (Hanna *et al.*, 2010).

Godrat Akhavanakbari et al. 2013 show a comparison of the effects of remifentanil and alfentanil on intraocular pressure in cataract surgery, the results of this study indicate the benefits of both remifentanil and alfentanil in managing IOP after induction and during anesthesia. It seems that remifentanil is better than alfentanil in controlling the IOP after injection of succinylcholine in doses of 1 µg/kg and 20 µg/kg respectively. This study is consistent with the results of our study (Akhavanakbari *et al.*, 2013). In 2015 Kasim Tuzcu et al. show in a comparative study the effects of remifentanil and esmolol on an increase in intraocular pressure due to laryngoscopy and tracheal intubation by measuring it before intubation and at 1, 3, 5, and 10 minutes after intubation. The study concluded that remifentanil is more effective than esmolol in preventing IOP elevation related to laryngoscopy and tracheal intubation. In our study, we investigate the effect of remifentanil vs placebo for the same purpose. In both studies, we use the same single dose of remifentanil (Tuzcu *et al.*, 2015).

According to this study remifentanil- propofol combination may be used as induction for G.A. in any emergency eye surgery including penetrating eye injury, and for patients with glaucoma scheduled for ophthalmic surgery as well with the use of succinylcholine to facilitate tracheal intubation.

5. CONCLUSION

Administration of remifentanil 1 µg/ kg after induction of anesthesia with propofol 2 mg/ kg prevents increasing in IOP associated with the administration of succinylcholine and tracheal intubation.

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Conflict of Interest

The authors declare that there are no conflicts of interests

Informed consent

Written informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval for human

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (Code: 2019/A079).

Author contribution

Haider Abbass Hassen: Conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and Drafting the work.

Iyad Abbas Salman: Conception and design of the work, interpretation of data for the work, and revising it critically for important intellectual content.

Mohammed Kassim A. Hassan: Conception and design of the work, and Drafting the work and finally revising it critically for important intellectual content.

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Data and materials Availability

All data associated with this study are present in the paper.

Peer-review

External peer-review was done through double-blind method.

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