Original Article

Increase in intraocular pressure is less with propofol and remifentanil than isoflurane with remifentanil during cataract surgery: A randomized controlled trial

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Abstract

Background: This double-blinded, randomized clinical trial was designed to evaluate intraocular pressure (IOP) change in cataract surgery using the combination of propofol and remifentanil or the combination of isoflurane and remifentanil.

Materials and Methods: One hundred sixty patients were randomly allocated to a maintenance anesthetic consisting of remifentanil + isoflurane (group I), normal saline + isoflurane (group II), propofol + remifentanil (group III) or normal saline + propofol (group IV). IOP was measured at seven predefined time points, baseline (T0), 3 min after the start of continuous remifentanil infusion (T2), after induction of anesthesia (T3), immediately after laryngoscopy and intubation (T4), 5 min after laryngoscopy (T5), immediately after the block of continuous remifentanil infusion (T6) and 3 min after T6 (T7). Outcomes included IOP, systole blood pressure (SBP) and diastole blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR).

Results: The mean of IOP in Group III was lower than other groups and in group IV was higher than other groups. At time point T4 and T5 differences in the mean of IOP between groups III and IV was significantly different ($P > 0.05$). The trend in changes in the mean of IOP was statistically significant among groups (P value $= 0.01$). The trends in changes in the mean of SBP, DBP and MAP were not significantly different among groups (P value $= 0.41$). HR in group III was significantly lower than other groups. The trend in changes in the mean of HR was significantly different among groups (P value $= 0.002$).

Conclusion: Propofol with remifentanil was more effective than placebo or adding remifentanil to isoflurane in management of IOP in cataract surgery.

Key Words: Cataract, intraocular pressure, isoflurane, propofol, remifentanil

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INTRODUCTION

A common cause of visual acuity loss is cataracts which reduced quality of life in the elderly population.[1] On a global scale cataract has been documented to be the most significant cause of bilateral blindness.[2] Cataract extraction is usually performed under regional eye block or general anesthesia. One of the problematic

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intraocular surgery operations for the surgeon is increasing intraocular pressure (IOP), so the elevation of IOP and controlling it in normal range is necessary.[3] IOP control before, during, and after the surgery is required for anesthesia management in ophthalmic surgery and one important aim in anesthetic management during ocular surgery is to provide adequate control of IOP.[4]

Ocular and visual function may impair postoperatively after large variations in IOP in open-system ocular surgery. Mechanical and pharmacological stress during surgery must be avoided because these procedures can contribute to an increase in IOP.[5,6] In general anesthesia in ocular surgery, short-acting anesthetic agents are commonly used. The central depressive effect on the diencephalic control of IOP, relaxing extraocular muscle tone and improving the aqueous humour outflow cause to reduce IOP in the use of most anesthetics.[7,8] It is shown that some agents such as propofol, thiopental, halothane, isoflurane and desflurane, fentanyl, alfentanil and remifentanil decrease IOP.[8-10]

Remifentanil is an ultra-short acting, nonspecific esterase-metabolized, selective mu-opioid receptor agonist, with a pharmacodynamic profile typical of opioid analgesic agents.[11] A combination of propofol with remifentanil is reported to decrease IOP after succinylcholine and tracheal intubation. And it has been shown that anesthetic regimens with sevoflurane and remifentanil are comparable to total intravenous anesthesia with propofol and remifentanil.[12,13]

There are no specific guidelines for prophylaxis in uncomplicated cataract surgery to minimize IOP rise and also prospective and controlled trials that used the combination of propofol and remifentanil or the combination of isoflurane and remifentanil in cataract surgery to manage IOP during surgery are limited and different. So, this randomized controlled clinical trial was aimed to evaluate IOP change in cataract surgery patients using the combination of propofol and remifentanil or the combination of isoflurane and remifentanil and to find a technique which is associated with minimal changes.

MATERIALS AND METHODS

This randomized, parallel-group, double-blind clinical trial was conducted between May and December 2013, on 180 patients who were scheduled for undergoing elective cataract surgery, under general anesthesia with tracheal intubation, in Faize hospital in Isfahan, Iran. Patients older than 18 years in both genders with American Society of Anesthesiologists classification I and II, without glaucoma and ophthalmic disease, no history of chronic disease, no history of surgery of the eye, no use of NSAIDs drugs up to 2 weeks before surgery were eligible. Also, patients were excluded from the study if they had known allergies; adverse reactions to any of the anesthetic agents used in the study; unstable angina or manifest congestive heart failure; if airway management was expected to be difficult. The ethics committee of Isfahan University of Medical Sciences approved this study, and written informed consent was obtained from all studied patients.

Eligible patients were randomly divided into four 40-member groups by Random Allocation software. Anesthesia in all patients was induced intravenously with remifentanil (1 mcg/kg), sodium thiopental (5 mg/kg) and atracurium (0.5 mg/kg). Balanced anesthesia in groups I and II was maintained using with isoflurane (1 mc/kg/min) and in groups III and IV was maintained using with propofol (100 mc/kg/min). So, patients in group I received isoflurane and infusion of remifentanil (0.1 mcg/kg/min), group II received isoflurane and normal saline, group III received propofol and infusion of remifentanil (0.1 mcg/kg/min), and patients in group IV received propofol and normal saline. Endotracheal intubation in all patients was performed with a single-lumen tube. Patients' lungs were mechanically ventilated with the same setting during ventilation (VT, 10 mL/kg and RR, 10 min). The patients were monitored and observed using an electrocardiogram, non-invasive arterial blood pressure device, and pulse oximeter. To maintain blinding, studied drugs were prepared in syringes in a double-blind fashion by a team member who was not involved in data recording and also patients were unaware of the treatment allocation.

Collected data included age, sex, weight, duration of surgery, duration of anesthesia, duration of recovery, IOP, systole blood pressure (SBP) and diastole blood pressure (DBP), mean arterial pressure (MAP) and heart rate which were assessed in all patients. A handheld applanation tonometer was used by an ophthalmologist to measure IOP contralateral to the operated eye. All measurements were taken singly with the patients in a horizontal position at nine predefined time points reported in Table 1.

Table 1: Time points for intraocular pressure measurement

T1 Baseline, before the start of continuous remifentanil infusion
T2 three min after the start of continuous remifentanil infusion
T3 after induction of anesthesia
T4 Immediately after laryngoscopy and intubation
T5 five min after laryngoscopy
T6 Immediately after the block of continuous remifentanil infusion
T7 three min after the block of continuous remifentanil infusion

All statistical analyses were done using SPSS software for Windows, version 20. Descriptive data are reported as mean ± SD or number (percent) as appropriate. One-way ANOVA with *post hoc* test and Chi-square test were used to compare all studied variables among groups as appropriate. Trend of studied variables at time points were compared between groups by repeated measurements of ANOVA. The level of significance is considered to be less than 0.05.

RESULTS

Figure 1 shows the flowchart of the study. Between July and January 2013, 195 patients were reviewed for eligibility. Twenty patients were not eligible and 15 refused informed consent and did not enter to the study. One hundred sixty patients were eligible and randomly assigned into four intervention groups. Finally, 134 patients completed the study and analyzed and 26 patients were excluded from the study. There were no significant differences between excluded patients and analyzed patients in any of the baseline variables (data not shown).

The mean age of the studied patients was 59.2 ± 12.1 years; 66 patients (60%) were females and 52 patients (40%) were males. Table 2 shows baseline characteristics of studied patients by groups. No significant differences were noted between intervention groups for mean of age and sex combination, weight, duration of anesthesia and duration of surgery ($P \geq 0.5$).

Figures 2 to 5 show the results of comparison of IOP, SBP, DBP, MAP, heart rate among study groups. During time points the mean of IOP in group III that received propofol and remifentanil was lower than other groups and in group IV that received propofol and normal saline was higher than other groups. IOP at time points T1, T2, T3, T6 and T7 was not significantly different among study groups ($P < 0.05$). At time point T4 and T5 differences in the mean of IOP between groups III and IV were significantly different ($P > 0.05$). The trend in changes in the mean of IOP was statistically significant among groups [P value = 0.01, Figure 2]. SBP at time point 3 and 4 in patients in group II was statistically more than in patients in group III ($P < 0.05$); also, at time point T3 patients in group II showed significant higher SBP than in patients in group IV (P value = 0.023). The trend in changes in the mean of SBP was not significantly different among groups [P value = 0.41, Figure 3]. The mean of DBP in group II at T3 was higher than in other groups and in group IV was lower than others, this difference between groups II and

Table 2: Baseline characteristics in studies patients by groups

Variables	Group I (*n*=32)	Group II (*n*=35)	Group III (*n*=31)	Group IV (*n*=36)	*P* value
Age (year)	54.2±12.3	60.6±13.9	58.7±13.4	62.7±7.1	0.06*
Weight	70.3±7.6	70.1±4.8	64.8±13.3	68.7±9.5	0.13*
Sex					
Male	13 (41)	20 (57)	14 (45)	13 (47)	0.31†
Female	19 (59)	15 (43)	17 (65)	23 (53)	
Duration of anesthesia (min)	49.8±6.8	52.6±12.2	48.8±7.9	53.1±10.1	0.3*
Duration of surgery (min)	35.6±5.8	36.8±8.3	34.2±7.9	38.9±7.1	0.11*

Data expressed as mean±SD or number (percent), group I, received maintained anesthesia with isoflurane then infusion of remifentanil (0.1 mcg/kg/min); group II, received maintained anesthesia with isoflurane then infusion of normal saline; group III, received maintained anesthesia with propofol then infusion of remifentanil (0.1 mcg/kg/min); group IV, received maintained anesthesia with propofol then infusion of normal saline, *P* values calculated by *one-way ANOVA, †Chi-square test

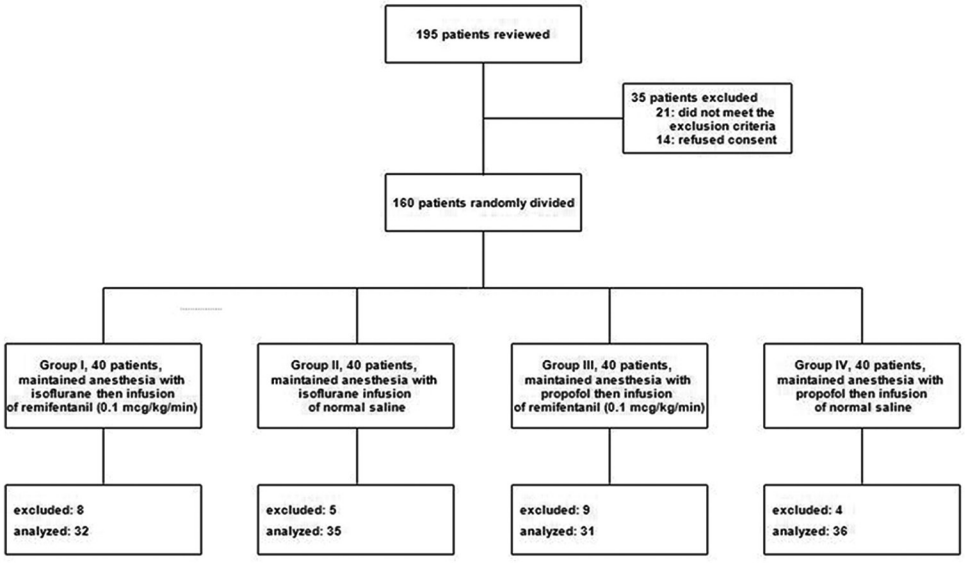

Figure 1: Flowchart of the study

IV was statistically significant (*P* values = 0.04). In other time points there was no significant difference among groups. The trend in changes in the mean of DBP was not significantly different among groups [*P* value = 0.27, Figure 4]. The mean of MAP in all time points was not significantly different among groups ($P > 0.05$); also, the trend in changes in the mean of MAP was not significantly different among groups [*P* value = 0.34, Figure 5]. The mean of heart rate in patients in group III, who received propofol and remifentanil, was significantly lower than other groups. The differences among groups I, II and IV for the mean of heart rate was not statistically significant. The trend in changes in the mean of heart rate was significantly different among groups [*P* value = 0.002, Figure 6].

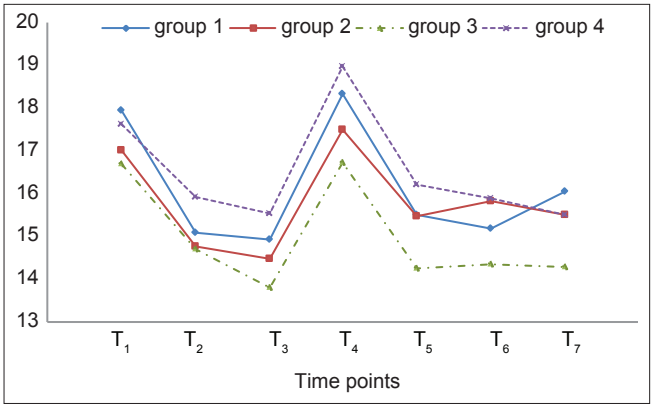

Figure 2: Comparison of intraocular pressure among study groups. Group 1, group isoflurane and remifentanil; group 2, group isoflurane and normal saline; group 3, group propofol and remifentanil; group 4, group propofol and normal saline, the difference between groups 3 and 4 at time points T4 and T5 were statistically significant (*$P < 0.05$). The difference of the trend of intraocular pressure was statistically significant among groups (*P*-value = 0.01)

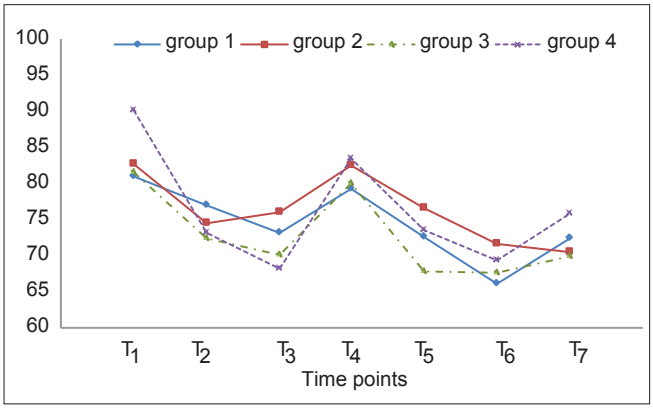

Figure 4: Comparison of diastolic blood pressure among study groups. Group 1, group isoflurane and remifentanil; group 2, group isoflurane and normal saline; group 3, group propofol and remifentanil; group 4, group propofol and normal saline, the difference at time point T3 between group 2 and 4 was statistically significant (**P*-values = 0.04). The difference of the trend of diastolic blood pressure was not statistically significant among groups (*P*-value = 0.27)

DISCUSSION

Around the world cataracts are one of the most frequent reasons for visual impairment that can cause progressively painless vision loss in very elderly patients.[14] The prevalence of cataracts in the population has increased due to the demographic shift in developed countries toward older age.[15] Increasing IOP during the surgery is a challenge that requires anesthesia management to control.[16] The present study as prospective, randomized study was conducted to compare the effects of isoflurane and propofol, both in combination with remifentanil, on IOP in cataracts surgery. Our findings showed that IOP in patients who received propofol and remifentanil from baseline to 3 min after infusion of remifentanil was

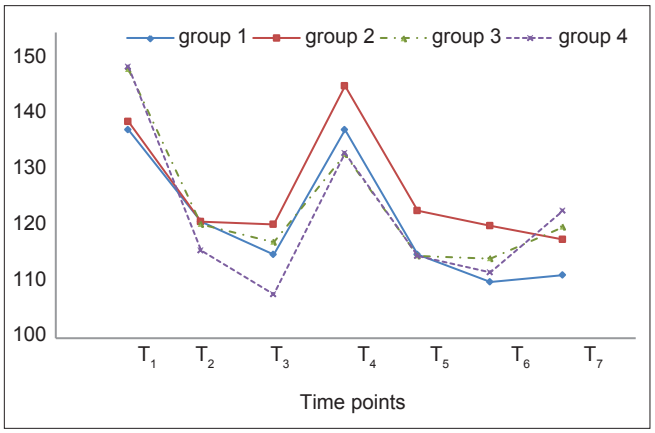

Figure 3: Comparison of systolic blood pressure among study groups. Group 1, group isoflurane and remifentanil; group 2, group isoflurane and normal saline; group 3, group propofol and remifentanil; group 4, group propofol and normal saline, the difference at time points T3 and T4 were statistically significant (**P* < 0.05). The difference of the trend of systolic blood pressure was not statistically significant among groups (*P*-value = 0.41)

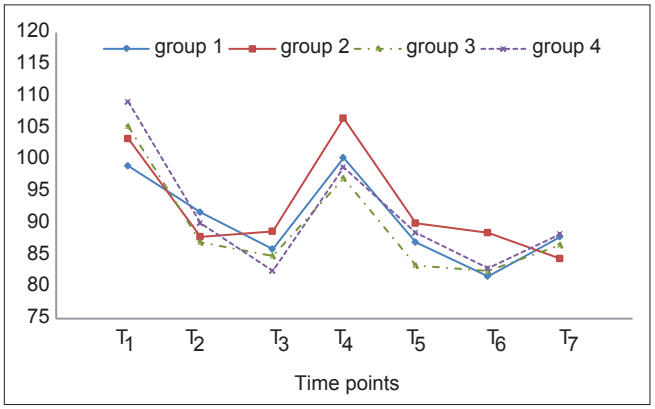

Figure 5: Comparison of MAP among study groups. Group 1, group isoflurane and remifentanil; group 2, group isoflurane and normal saline; group 3, group propofol and remifentanil; group 4, group propofol and normal saline, the difference at time points among groups was not statistically significant ($P > 0.05$). The difference of the trend of MAP was not statistically significant among groups (*P*-value = 0.34)

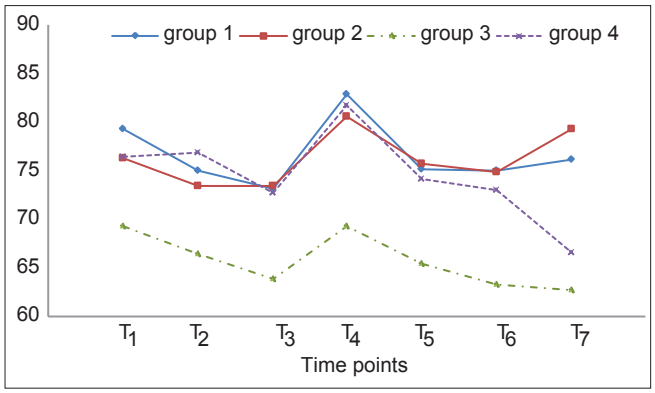

Figure 6: Comparison of heart rate among study groups. Group I, group isoflurane and remifentanil; group 2, group isoflurane and normal saline; group 3, group propofol and remifentanil; group 4, group propofol and normal saline, the difference in all time points was statistically significant ($P < 0.05$). The difference of the trend of heart rate was statistically significant among groups (P-value = 0.002)

significantly lower than normal saline group. These results demonstrated that adding remifentanil to propofol was more effective than placebo or adding remifentanil to isoflurane in management of IOP in cataract surgery. Also, patients who received propofol and remifentanil were more stable than other groups in term of SBP, DBP, MAP and heart rate although there were no significant differences among groups in all time points.

It is reported that most anesthetic drugs, including i.v. anesthetics, volatile agents and muscle relaxants, reduce IOP,[17] but studies that have yet assessed the effect of isoflurane and propofol, both in combination with remifentanil, on IOP in humans are limited; in a study by Schäfer *et al.*,[18] 40 patients scheduled for elective cataract surgery were assessed in a prospective, randomized study to compare the effect of sevoflurane and propofol, in combination with remifentanil, on IOP. They found that during and following the induction of anesthesia, IOP was reduced in both groups, and reported IOP was significantly lower in the propofol group than in the sevoflurane group during the induction of anesthesia. Also, they concluded that in patients undergoing cataract surgery under general anesthesia with tracheal intubation, anesthetic regimens with propofol as well as with sevoflurane, both combined with remifentanil, decrease IOP significantly; however, in the propofol group the decrease in IOP was significantly more pronounced than in the sevoflurane group. Similar to the results of Schäfer *et al.*[18] study we found that IOP was reduced in both groups that received isoflurane or propofol, both in combination with remifentanil, during and following the induction of anesthesia; also, anesthetic regimens with propofol and remifentanil were better than anesthetic regimens with isoflurane and remifentanil and isoflurane or propofol both in combination with normal saline.

In another study 66 patients were randomly allocated to a maintenance anesthetic consisting of remifentanil and sevoflurane or remifentanil and propofol. IOP in this study was measured at nine predefined time points. This study showed that propofol-based total intravenous anesthesia is more effective than sevoflurane-based inhalation anesthesia in reducing IOP increase during robot-assisted laparoscopic radical prostatectomy with pneumoperitoneum and steep Trendelenberg.[19] Other study by Mowafi *et al.*[20] showed that propofol-based total intravenous anesthesia was superior to isoflurane inhalation anesthesia in reducing the increase in IOP during laparoscopic surgery in the Trendelenberg position. Similar to Yoo *et al.*[18] and Mowafi *et al.*,[20] our results showed that propofol was superior to isoflurane inhalation anesthesia in reducing the increase in IOP during cataracts surgery. In our study like Yoo *et al.*[18] IOP in all studied groups decreased during cataracts surgery whereas Mowafi *et al.*[20] reported that the significant increase in IOPs was observed with isoflurane anesthesia in their study. This discrepancy between studies seems to be due to the difference in the study population. Mowafi *et al.*[20] study conducted in young female patients with a mean age of 31 year and baseline mean of IOP found to be within the normal range in all studied patients (<20 mmHg). Yoo *et al.*'s[18] study was conducted on patients older than 60 year while studied patients in the present study were between 23 and 75 years age.

Based on the results, it can only be assumed that propofol with remifentanil may have a greater ability to alleviate adrenergic stimulation and thus maintain IOP at a lower level. The more marked and sustained decrease in IOP in the propofol group compared with the isoflurane group may be explained that propofol is better in blocking the sympathetic response during endotracheal intubation and extubation than isoflurane. However, MAP and heart rate are the only parameters for the depth of anesthesia[21] and our results showed that no differences occurred among the groups for MAP but in propofol with remifentanil was more effective than other anesthetic regimens to reducing heart rate increase during cataracts surgery.

The possible main limitation of our study is that 26 patients who were allocated to study groups were exclude during the study although there were no significant differences between excluded patients and analyzed patients in any of baseline variables but decrease in the number of patients in final analyses would have been a possible cause of bias and can

effect on the power of the study to clear the differences between groups.

In conclusion, results of our study show that propofol in combination with remifentanil was more effective than placebo or adding remifentanil to isoflurane in management of IOP in cataract surgery and overall the use of propofol in combination with remifentanil may be of benefit in this patient population. However, further studies are need to be done.

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