Original Article

Comparison of Sedation Quality and Pain with Propofol-Thiopental Sodium versus Propofol-Etomidate in Cataract Surgery

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ABSTRACT

Purpose: To compare the effectiveness of Propofol + Sodium thiopental (Thiofol) versus Propofol + Etomidate (Etofol) in achieving a more favorable sedation during phacoemulsification.

Study Design: Randomized controlled trial.

Place and Duration of Study: Feyz Hospital, an ophthalmology referral center in Isfahan province from January 2022 to November 2022.

Methods: A total of 64 patients (25 females and 39 males) were assessed with an average age of 65.14±13.34 years. Patients who underwent elective phacoemulsification operation under sedation and were randomly divided into the Propofol+Sodium thiopental (Thiofol) and Propofol+Etomidate (Etofol) groups. There were 32 patients in each group. Demographic information, sedation level, medical condition, anesthetic complications, hemodynamic parameters prior to, during, and following the operation, and the visual analog scale (VAS) were measured by an anesthesiologist and compared.

Results: The groups showed significant differences in the levels of Ramsay scores (P<0.001). The frequency of Ramsay scores 2 and 3 was 43.75%, 56.25%, and 0%, 100% in Etofol, and Thiofol groups, respectively. The average recovery time showed a significant increase in the Etofol group compared to the Thiofol group (P<0.001); the VAS in the Thiofol group showed a significant rise compared to the Etofol group (P <0.001).

Conclusions: Although the sedation quality while phacoemulsification cataract surgery was acceptable with both drugs and the results between groups were not significantly different considering recovery time and pain control, recovery time was less in Etofol and pain control was more effective in Thiofol.

Key Words: Sedation, Etomidate, Sodium thiopental, Phacoemulsification.

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INTRODUCTION

Anesthesia is one of the most vital parts of any surgery that can determine comfort, life and death of a patient. Many drugs are used for anesthesia, each of which has its side effects and benefits.[1,2] There are many surgeries in developing or developed countries, which are performed under general anesthesia.[3] Although most of the ocular surgeries are performed under local anesthesia, cataract surgery is one of the surgeries which requires general anesthesia in some cases. However, if the patient is old or has risk factors not favoring general anesthesia, the patient's pain can be relieved with sedative drugs. Etofol, Propofol, Sodium thiopental and Midazolam can be used for patients

who require sedatives for their cataract surgery. Medications such as Midazolam, Fentanyl, Atracurium and Pentothal are used for patients who undergo general anesthesia during this surgery.[4-7]

There are post-operative complications associated with the use of anesthetic drugs. One of the critical complications that can be observed after surgery is an increase in blood pressure. Patients with a history of high blood pressure and suffering from psychosis, stress, and mania can be prone to increased blood pressure during and after the operation. In patients who undergo surgery with general anesthesia, the control of vital signs such as blood pressure and heart rate playan essential role in controlling patient's condition.[8-10]

Propofol-Thiopental sodium and Etofol are relatively common medications used for anesthesia. However, studies comparing these two therapeutic compounds do not provide a conclusive evidence requiring more studies to draw a useful conclusion.[11-13] We planned this study to evaluate these drugs in terms of effect on vital signs and examinations and the number of post-operative complications according to their anesthetic regimen.

METHODS

This randomized, controlled, clinical trial was conducted in Faiz Hospital, an ophthalmology referral center, in Isfahan, Iran, affiliated with the Isfahan University of Medical Sciences. Approval was obtained from the Ethics Committee (IR.MUI.MED.REC.1399.650) and Department of Anesthesiology Isfahan University of Medical Sciences and the research was registered in the Iranian Clinical Trials Registry (IRCT20160307026950N37).

Patients who provided consent to be included in the study, age over 18 years and candidates for cataract surgery were included. Patients with a history of mental disorders, nystagmus, leukemia, epilepsy, deafness, or drug allergies were excluded. Patients with severe hemodynamic disorder, sensitivity to these drugs, patient's non-cooperation and withdrawal from the study were also excluded.

Sample size was calculated as follows:[14]

$$n = \frac{2 \times SD^2 (\frac{Z\alpha}{2} + \frac{Z\beta}{2})^2}{d^2}$$

Where SD = Pooled standard deviation, $Z_{\alpha/2} = Z_{0.005/2}$ = 1.96 at Type I error, $Z_{\beta} = Z_{0.20}$ = 0.84 at 80% power, d = effect size = difference between two mean

$$n = \frac{2 \times (31.82)^2 \times 7.84}{28^2}$$

Minimum sample size required was 21. We included 32 patients in each group. The patients were informed about the research method and objectives and signed written informed consent. The selected patients were randomly divided into two groups using random assignment software to receive Thiofol and Etofol. An anesthesiologist blinded to the groups noted their demographic information and medical status. Hemodynamic parameters prior to, during, and following the operation, level of sedation, complications of anesthesia, side effects caused by sedation, and satisfaction of surgeons and patients were measured by an anesthesiologist and compared.

Pulse oximetry, Electrocardiography (ECG), capnography, and automatic non-invasive blood pressure monitoring were conducted prior to and during the operation. Patients were given 4 L/min of oxygen through nose. Diastolic and Systolic blood pressure, blood oxygen saturation (SpO^2), and heart rate (HR) were assessed before induction of sedation, one minute later during surgery, 5 min later during surgery, and every 10 minutes during the operation and in the recovery room. In every patient, Propofol was injected at 10 mg; in the Thiofol group, patients received Thiofol at 1 mg/kg, and in the Etofol group, patients received Etomidate at 0.3 mg/kg. Anesthesia complications included tachycardia, bradycardia, hypotension, hypoxemia, hypertension, apnea, myoclonus, SpO2 less than 90%, restlessness, nausea, and vomiting after the operation treated by a blinded anesthesiologist to the groups. The interval from the end of the operation to meeting the discharge criteria from the post-anesthesia care unit was noted. Patients' improvement was evaluated using the modified Aldrete score (MSA). Based on the activity, SpO2, alertness, breathing, and blood circulation were scored from 0 to 10. Those who achieved an Aldrete score of 9 – 10 were discharged.[15]

For measurement of Acute Pain, we used a visual analog scale. It is a subjective and valid measure for chronic and acute pain. Scores are recorded by creating a scale on a 10 cm line representing a continuum from zero "no pain" to 10 "worst pain".[16]

Ramsay sedation score was used to measure the

quality of sedation. According to this criterion, numbers 1 to 6 are assigned to it, and number 1 indicates the patient is anxious and agitated and number 6 indicates that patient does not respond to pain.[17]

SPSS 26 was used for data analyses. The qualitative and quantitative variables were expressed respectively as number (percentage) and mean (SD).In order to analyze the data, we used independent T-tests and analysis of variance if the data was parametric. The significance level in the tests was considered to be 0.05.

RESULTS

Of 125 patients, 61 cases were excluded (50 cases did not meet our criteria and 11 cases did not sign informed consent). According to the inclusion criteria, 64 cases were randomly divided into two groups (Figure 1). A total of 64 patients (25 females and 39 males) were assessed with an average age of 65.14±13.34 years. Table 1 indicates their demographic characteristics. The groups showed no significant differences in mean age, height, and weight (P > 0.05) (Table 1).

Tables 2 and 3 indicate the operative details of the subjects in the groups prior to, during, and following the procedure.

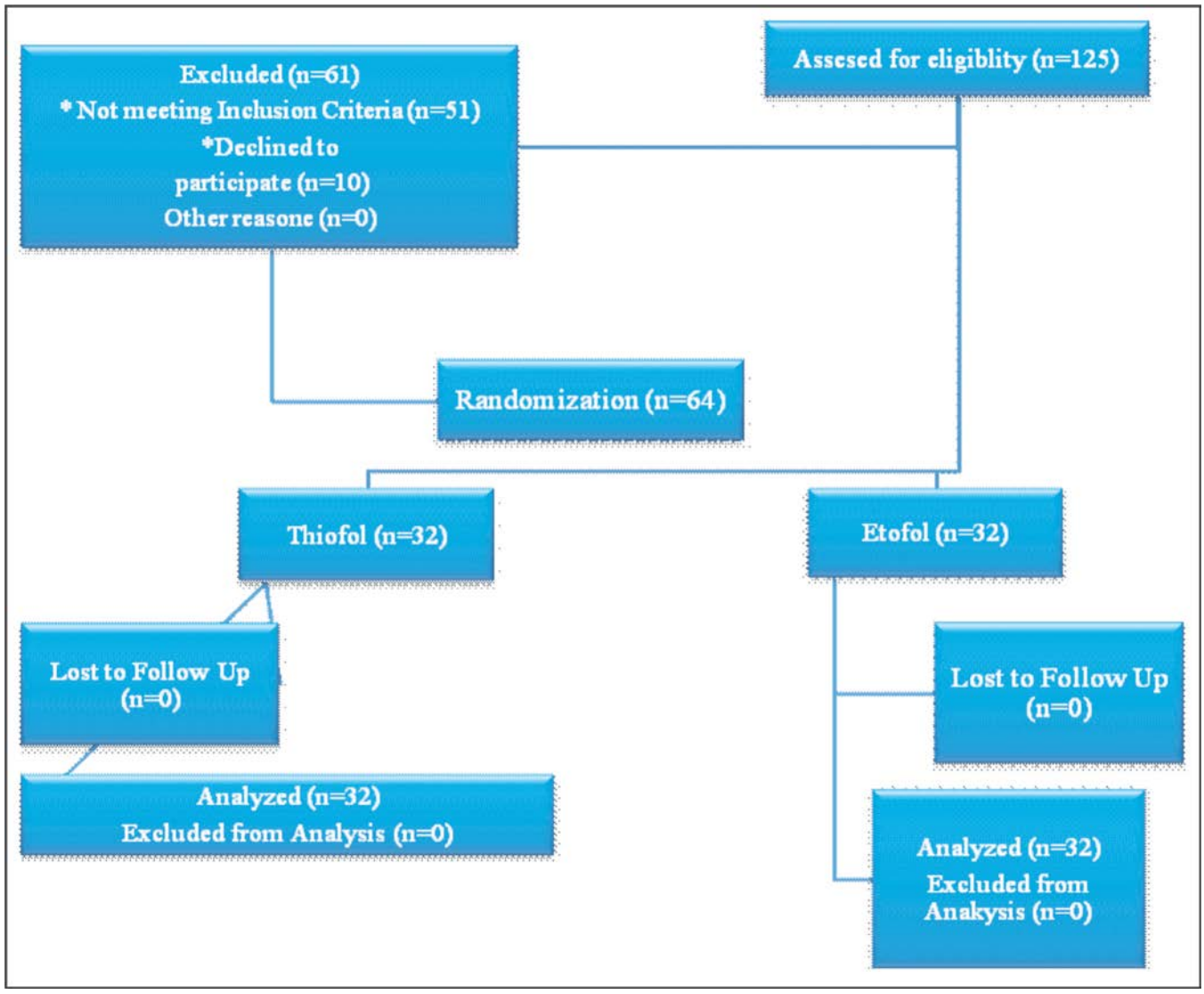

Figure1: Consort diagram for the study.

Ramsay scores was found with a significant difference between the groups (P<0.001). The frequency of Ramsay scores of 2 and 3 was 43.75%, 56.25%, in Etofol, and 100 % in Thiofol groups for score of 3, respectively.

The Thiofol group showed significantly higher mean recovery time than the Etofol group (P<0.001). Before and after surgery, the groups showed no different hemodynamic characteristics but during surgery, we observed a significant difference between the Thiofol and Etofol groups in Diastolic, Systolic, and Mean arterial blood pressure (respectively P=0.001 and P<0.001). One minute and five minutes after starting surgery we observed a significant sudden drop in blood pressure. The groups showed no significant difference in SpO2 during surgery and no anesthesia related complications. The Visual Analog Scale (VAS) in the two studied groups is presented in Figure 2 and the groups showed significant differences (P<0.001).

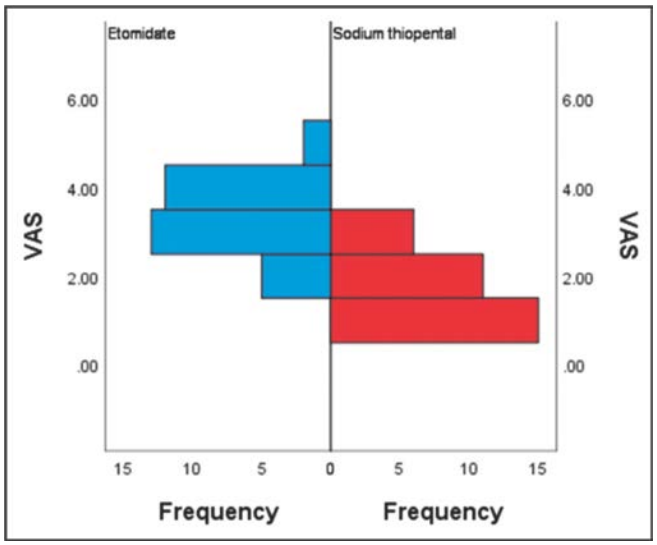

Figure 2: Visual Analog Scale (VAS) in the study groups.

Table 1: *Demographic Characteristics of Patients in the Study Groups*

Variable	Thiofol, N=32	Etofol, N =32
Age, y	64.28±11.43	66±15.15
Gender, female/male	14/18	11/21
Weight, kg	65.59±10.76	64.87±8
Height, cm	165.09±7.1	165.71±7.87

Table 2: *Operative Details of Patients Before, During, and After the Procedure in the Study Groups.*

	Variable	Thiofol, N=32	Etofol, N =32	*P Value
	Pulse rate	78.18±6.39	77.03±9.88	0.790
	Blood pressure			
	Systolic	133.87±11.22	137.34±10.52	0.220
	Diastolic	77.09±6.69	80.15±10.29	0.114
	Mean arterial blood pressure	152.69±15.14	156.38±13.96	0.256
	Arterial oxygen saturation	96.15±1.90	95.56±3.91	1.00
During Surgery	Ramsay score			**<0.0001**
	1	0 (0)	0 (0)	
	2	0 (0)	14 (43.75)	
	3	32 (100)	18 (56.25)	
	4	0 (0)	0 (0)	
	5	0 (0)	0 (0)	
	6	0 (0)	0 (0)	
	Pulse rate	78.53±9.60	76.97±13.07	0.598
	Blood pressure			
	Systolic	127.09±9.91	134.91±11.14	**0.001**
	Diastolic	75.75±6.00	82.47±8.18	**<0.001**
	Mean arterial blood pressure	92.84±5.74	99.91±8.82	**<0.001**
	Arterial oxygen saturation	99.87±0.33	99.28±0.95	0.088
After Surgery and Recovery	Recovery time	57.18±12.11	29.06±7.23	**<0.001**
	Anesthesia time	26.40±6.50	27.50±7.51	0.631
	Surgery time	20.93±6.40	21.71±7.14	0.768
	Pulse rate	72.03±7.67	71.21±10.75	0.391
	Blood pressure			
	Systolic	131.81±2.21	131.09±12.31	0.818
	Diastolic	77.81±8.35	76.43±10.40	0.493
	Mean arterial blood pressure	95.78±8.52	94.63±7.98	0.957
	Arterial oxygen saturation	98.37±1.18	97.78±1.60	0.123

Table 3: *Anesthetic complications of Patients Before, During and After the Procedure in the Study Groups.*

Variable	Thiopental N=32	Etofol N =32	*P Value
Dizziness	0	0	-
Restlessness	0	0	-
Vomiting	0	0	-
Nausea	0	0	-
Hypertension	8 (25)	5 (15.62)	0.351
Bradycardia	0	0	-
Tachycardia	2 (6.25)	1 (3.12)	0.554
Hypotension	0	0	-

*Mann–Whitney U test. $p<0.05$, Data presented as Mean ± Standard Deviation and No. (%)

DISCUSSION

In the present study, the mean recovery time in the Etofol group was significantly shorter compared to the Thiofol group. Our results are consistent with those of Banihashem et al, who reported significantly shorter recovery time in the Etomidate-Fentanyl group compared to the Propofol-Fentanyl group.[17] Toklu et al, found a shorter recovery time for Etomidate compared to Propofol during colonoscopy.[18] Our findings are consistent with those of Moerman et al, reporting a shorter recovery time for Propofol following the cardioversion procedure compared to Etomidate.[19]

A higher sedation score is related to a shorter recovery time. According to Toklu et al, the Ramsay sedation scores of 3-4 had a similar frequency in those receiving elective colonoscopy using Propofol-remifentanil and Etomidate-remifentanil combinations.[18] Hemodynamic assessment at baseline, and after surgery showed a significant difference between our groups but during surgery, we observed a significant difference between the Thiofol and Etofol group in Systolic, Diastolic, and Mean arterial blood pressure before and after injection, in such a way that Thiofol caused a drop in blood pressure. Possibly Etomidate cannot inhibit myocardial function or sympathetic tone. In contrast with this research, Aghadavoudi et al, compared the effects of Etomidate infusion and Ketamine +Fentanyl +midazolam on sedation quality during cataract surgery and reported a significant increase in the pulse rate and hemodynamic changes after recovery.[20] The Etomidate and Fentanyl group showed a significant decrease in hemodynamic fluctuations. Different findings can be related to variations in the doses, surgery length, and use of a sedative drug in infusion or bolus.

In this study average diastolic and systolic blood pressure and average arterial blood pressure values were similar to the research conducted by Di Liddo et al, investigating the effects of midazolam and Etomidate on pediatric outpatient surgeries, in which diastolic and systolic blood pressure levels showed no significant difference in the Etomidate group.[21]

Inter- and intragroup comparisons indicated no significant alterations in SpO_2 during the surgery. Aghadavoudi et al, reported significantly higher SpO_2 in the Etomidate-Fentanyl group, particularly following recovery compared to the Ketamine+ Fentanyl +midazolam group, which is not in line with our findings.[20]

The groups showed no significant differences in anesthetic complications. The commonest complication after surgery in the two groups was hypertension. Though it was not significantly different, it showed a lower frequency in the Etomidate group.

We observed a slight difference among the groups in the VAS so that VAS in the Thiofol group was better than the Etofol group, although VAS in both was in good range. In contrast to this study, Vedat Çakırtekin et al, compared the impact of thiopental sodium and propofol on hemodynamics, awareness, and newborns during caesarean section under general anesthesia with no significant differences between the groups in the systolic and diastolic arterial pressure, mean arterial pressure, HR, SpO2 and VAS measurements at the 1st hour postoperatively.[22] Erkman Sanri et al, compared Etomidate/Fentanyl (etofen) and Ketamine/Propofol (ketofol) combinations for analgesia and procedural sedation in the emergency department, and there was a significant difference between groups in VAS measurements in all stages of experiment.[23]

CONCLUSION

The findings of the present study showed that the sedation quality during cataract surgery was acceptable in both anesthetic drugs and did not show significant differences between groups. However, regarding other factors, such as recovery time, it is recommended that although Etofol significantly reduced the recovery time, Thiofol was more effective in reducing pain. However, the authors of this article believe that anesthesiologists, considering the physical status of the patient (ASA), are autonomous in

choosing between these two drugs, taking into account the physical condition of the patient and preoperative anesthesia examinations at the pre-operative clinic.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(IR.MUI.MED.REC.1399.650).**

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Authors' Designation and Contribution

Behzad Nazemroaya; Anesthesiologist: *Concepts, Design, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Review.*

Hamidreza Shetabi; Anesthesiologist: *Concepts, Data Acquisition, Manuscript Editing, Manuscript Review.*

Darush Moradi Farsani; Anesthesiologist: *Literature Search, Data Analysis, Manuscript Review.*

Ali Ariya; Anesthesiologist: *Literature Search, Manuscript Editing.*