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ORIGINAL RESEARCH

Successful Use of Low-Dose Combination Propofol and Fentanyl in Cataract Surgery Phacoemulsification

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Background: The combination between sedatives and opioids is one of the recommended anesthetic options in ophthalmic procedures and regimens are more advantageous as smaller amounts of each drug can be administered to reduce side effects and have proper outcomes due to the synergistic effects. This study aims to observe the use of low-dose propofol and fentanyl for patients undergoing phacoemulsification surgery.

Material and Methods: This observational study involves a sample of 125 adult patients who underwent elective cataract procedures using the phacoemulsification technique and had an American Society of Anesthesiologists (ASA) physical status of 1 to 3. Dose amount of fentanyl and propofol, Ramsay score, hemodynamic parameter, side effects, and patient satisfaction were evaluated, recorded, and analyzed using a 5-point Likert scale.

Results: The result showed the mean absolute dose of propofol was 12.46±4.376 mg, with a range between 10 and 30 mg, while the mean per body weight was 0.21±0.075 mg. Similarly, the mean absolute dose for fentanyl was 25.04±3.012 mcg within the range of 10–50 mcg, and the per-body weight dose was 0.43±0.080 mcg. About 90.4% and 9.6% of the patients reached Ramsay 2 and 3, respectively. The analysis of systolic, diastolic blood pressure, mean arterial pressure, and pulse rate showed that the combination of low-dose fentanyl and propofol was significantly lower than before therapy administration in all four values ($p < 0.05$).

Conclusion: The combination of low-dose propofol and fentanyl in cataract surgery using phacoemulsification successfully reached the targeted sedation level and a significant decrease in blood pressure, MAP, pulse rate, minimal side effects, and high satisfaction rate.

Keywords: combination, propofol, fentanyl, low dose, phacoemulsification, sedation

Introduction

According to the 2010 Global Burden of Disease Study and other worldwide meta-analyses, 32.4 million individuals worldwide were blind. Globally, the leading overall cause of blindness was cataracts. The only treatment for cataracts is surgery. Phacoemulsification is the gold standard for cataract surgery in the developed world. The benefit of phacoemulsification over purely manual methods is the ability to extract the large nucleus through a small incision of ≤3.0mm[1] There is no anesthesia gold standard for cataract surgery,[2] however, having safe, painless, efficient, and effective anesthesia is the goal, regardless of the decision.[3] The trend has shifted in cataract surgery from general anesthesia to the combination of sedation and topical anesthesia.[4]

Fear and anxiety directly related to the procedure are well-known preoperative feelings for patients scheduled to undergo cataract surgery.[5] Counselling is not only to provide information and clarify the patient's doubts but also to reassure them. Ophthalmologists and other health-care professionals can contribute to improving communication with patients.[6] Catecholamine release induced by anxiety has a negative effect on comorbidities, which are present in many

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cataract patients. Anxiolysis can also reduce catecholamine secretion and subsequently tachycardia and hypertension.[7] Meanwhile, the major predictors of lower patient satisfaction with ocular surgery include pain, fear, and anxiety.[8]

One of the recommended options in ophthalmic procedures, which could have proper outcomes due to the synergistic effects of these agents is the combination between sedatives and opioids. Several studies have demonstrated the effectiveness of different combination therapies to achieve conscious sedation during cataract surgery under local anesthesia. The combination of sedatives and opioids provides better sedation during phacoemulsification due to its favorable effects.[9] Combined regimens are more advantageous as smaller amounts of each drug can be administered to reduce side effects.[7]

The ideal sedative agent is non-toxic, has a rapid onset and short duration of action, has a favorable therapeutic index and predictable effects, does not cumulate, and is cost-effective.[2] Unfortunately, no drug is presently available that fulfills all these criteria.[7] Fentanyl citrate is a narcotic analgesic that has been extensively used in ophthalmic procedures under topical anesthesia, which includes cataract surgery.[10] It is 50 to 100 times more potent than morphine and has a quick onset of action and predictable short duration but less sedative effect.[9] The effects of these drugs in excess doses besides sedation are nausea and vomiting.[11] Fentanyl is the most commonly used opioid due to its ease of administration, but the time-to-peak effect is relatively slow.[12]

Sedative drugs are abundant, one of which is propofol, used for sedation and also for hypnosis. It is preferred for moderate-to-deep sedation due to its easy titration, allows a more rapid recovery of cognitive function, and has antiemetic properties.[13] Its major side effects include respiratory depression and reduced blood pressure. However, administering this drug at a lower dose is suggested for safe medication. Meanwhile, propofol lacks analgesic properties,[11] and must be combined with analgesics for painful procedures.[12] A previous study compared the use of a combination of fentanyl with etomidate, propofol, and midazolam, which concluded that the patients' mean score of satisfaction in the propofol group was significantly higher than the etomidate.[14] Any increase in blood pressure during surgery can lead to ocular and systemic complications such as suprachoroidal hemorrhage, stroke, or myocardial ischemic events. The blood pressure changes in phacoemulsification surgery may require constant monitoring for achieving favorable ocular and systemic outcomes.[15]

Administering drug at a lower dose decreases the possibility of side effect to occur. This study aims to observe the use of low-dose propofol and fentanyl for patients undergoing phacoemulsification. It also analyzes the effect of the combination therapy on sedation level using the Ramsay scale, systolic and diastolic blood pressure, mean arterial pressure (MAP), heart rate, side effects, and patient satisfaction rate on a five-point Likert scale.

Method

This is an observational study with all samples that meet the inclusion criteria and signed informed consent to participate will be included as the subjects. The consecutive sampling method was used to collect data from all patients that underwent cataract surgery with the phacoemulsification technique from February to April 2021 and signed informed consent. The current study protocol was approved by the Ethics Committee of National Eye Center Cicendo Eye Hospital of Medical Sciences with ethical approval letter number LB.02.01/2.3/017/2021. Furthermore, written informed consent was obtained from each subject. The study was conducted on adult patients and it followed the tenets of the Declaration of Helsinki. All adult patients who underwent elective cataract procedures using the phacoemulsification technique had an American Society of Anesthesiologists (ASA) physical status of 1 to 3. The exclusion criteria include patients who had involuntary movements such as Parkinson's disease, were mentally disabled, and had already received sedatives and analgesia preoperative. Drop-out criteria were intraoperative procedure complications such as lens nucleus or intraocular lens drop, and all patients who received additional sedatives other than fentanyl and propofol during the procedure.

The age, gender, weight, comorbidities, and ASA physical status of all subjects were recorded. Hemodynamic parameters before and during surgery, sedation level using the Ramsay scale summarized in Table 1, doses of fentanyl and propofol, side effects, and patient satisfaction after surgery, immediately after the patients entering the recovery room were evaluated and recorded using a five-point Likert scale.

The patients underwent noninvasive blood pressure monitoring, electrocardiography (ECG), and pulse oximetry and they also received oxygen of 3 liters per minute via nasal cannula before and during the procedure. Anesthesia with topical eye drops (tetracaine 2%) was given before surgery. Surgery is performed by an experienced surgeon or trainee. Subsequently, the subjects were given fentanyl, and after two minutes, the patients received propofol for sedation.

Table 1 Ramsay Sedation Scale

Level of Response	Ramsay Sedation Scale
1	The patient is anxious and agitated or restless or both
2	The patient is cooperative, oriented, and tranquil
3	Patient response to commands only
4	The patient exhibits a brisk response to a light glabellar tap or loud auditory stimulus
5	The patient exhibits a sluggish response to a light glabellar tap or loud auditory stimulus
6	The patient response shows no response

Note: Data from Ramsay et al.[16]

Intraoperatively, the heart rate, blood pressure, mean arterial pressure, and saturation were monitored regularly. Subsequently, data were analyzed to determine the effect of fentanyl and propofol combination on systolic and diastolic pressure, MAP, and heart rate. For data analysis, the paired *t*-test is performed for normally distributed data; otherwise, the Wilcoxon test is performed. Results were considered statistically significant when $p < 0.05$.

After the procedure, patients were then shifted to recovery from the operative room. Complications during recovery were recorded, and all patients were asked for sedation satisfaction immediately after the patients entering recovery room using a five-point Likert scale namely 1 (Not Satisfied), 2 (Not too Satisfied), 3 (Average), 4 (Satisfied), 5 (Very Satisfied).[17]

Results

A total of 125 subjects were included in this study. Table 2 describes patient characteristics such as age, sex, weight, comorbidities, duration of operation, and the American Society of Anesthesiologists (ASA) score. The result showed that the use of propofol and fentanyl with a mean absolute dose of 12.46±4.376 mg and 25.04±3.012 mcg or mean per body weight dose of 0.21±0.075mg/kg and 43±0.080 mcg/kg, respectively, achieved Ramsay score of 2 in most patients (113 or 90.4%) as described in Table 3. The results of systolic blood pressure analysis using a paired *t*-test, and diastolic blood pressure, mean arterial pressure (MAP), and pulse rate using the Wilcoxon test showed that the four values after the use of the combination of fentanyl and propofol were significantly lower than before therapy administration ($p < 0.05$) as portrayed in Table 4. Most of the patients had no complications (113 or 90.4%), with a satisfaction rate of 4.136 based on the Likert scale as shown in Table 5.

Table 2 Demographic Characteristics

Variable	N=125
Age (years)	
Mean±Std	64.00±12.291
Median	65.00
Range (min-max)	30.00–88.00
Sex	
Male	53 (42.4%)
Female	72 (57.6%)
Weight (kg)	
Mean±Std	59.70±11.118

(*Continued*)

Table 2 (Continued).

Variable	N=125
Median	60.00
Range (min-max)	35.00–98.00
Comorbidities	
Hypertension	68 (54.4%)
Diabetes Mellitus	18 (14.4%)
Others	37 (29.6%)
Duration of operation (minute)	
Mean±Std	23.83±10.467
Median	25.00
Range (min-max)	5.00–58.00
ASA	
1	14 (11.2%)
2	68 (54.4%)
3	43 (34.4%)

Abbreviation: ASA, American Society of Anesthesiologist score.

Table 3 Dose of Propofol, Fentanyl, and Ramsay Score

Variable	N=125
Propofol Absolute Dose (mg)	
Mean±Std	12.46±4.376
Median	10.00
Range (min-max)	10.00–30.00
Propofol Dose Per Body Weight (mg)	
Mean±Std	0.21±0.075
Median	0.18
Range (min-max)	0.11–0.44
Fentanyl Absolute Dose (mcg)	
Mean±Std	25.04±3.012
Median	25.00
Range (min-max)	10.00–50.00
Fentanyl Dose Per Body Weight (mcg)	
Mean±Std	0.43±0.080
Median	0.42

(*Continued*)

Table 3 (Continued).

Variable	N=125
Range (min-max)	0.19–0.71
Ramsay Score	
2	113 (90.4%)
3	12 (9.6%)

Table 4 Comparison Between Systolic Blood Pressure, Diastolic Blood Pressure, MAP, and Pulse Rate Before Administration of Fentanyl-Propofol with 5 Minutes Post-Administration of Fentanyl-Propofol

Variable	Pre-Administration of Fentanyl-Propofol	5 Minutes Post Administration of Fentanyl-Propofol	*P* value
	N=125	N=125	
Systolic Blood Pressure (mmHg)			0.0001*
Mean±Std	152.89±17.502	143.74±16.448	
Median	152.00	143.00	
Range (min-max)	108.00–227.00	105.00–196.00	
Diastolic Blood Pressure (mmHg)			0.0001*
Mean±Std	88.22±10.547	83.78±10.849	
Median	88.00	83.00	
Range (min-max)	62.00–119.00	58.00–115.00	
MAP (mmHg)			0.0001*
Mean±Std	109.77±11.456	103.76±11.301	
Median	108.33	102.33	
Range (min-max)	79.33–145.67	73.67–140.00	
Heart Rate (min-1)			0.0001*
Mean±Std	77.66±15.695	73.84±14.944	
Median	76.00	72.00	
Range (min-max)	47.00–133.00	42.00–137.00	

Notes: The *Sign indicates the value of p<0.05, which means that it is statistically significant.
Abbreviation: MAP, mean arterial pressure.

Discussion

Dose of Combination Therapy

Monitoring anesthetic care (MAC) or sedation can alleviate anxiety and analgesia, which will increase patients' satisfaction. Furthermore, the patients who undergo cataract surgery are usually elderly and have comorbidities and painful stimuli during operations.[18] The use of sedation for patients undergoing cataract surgical procedures during local/regional anesthesia strikes a balance between patient comfort, safety, and an optimal outcome.[19] It is achieved through the use of sedatives and analgesics to induce drowsiness and alleviate fear, anxiety, and pain.[7]

Table 5 Side Effects Dan Patient Satisfaction

Variable	N=125
Side effect	
No complaint	113 (90.4%)
Drowsiness	8 (6.4%)
Light Pain	4 (3.2%)
Patient Satisfaction Based on the Likert Scale	
3	6 (4.8%)
4	96 (76.8%)
5	23 (18.4%)

A previous study found that the administration of fentanyl at 0.75 mcg/kg in patients over 65 years old in combination with 0.5 mg/kg propofol provided good quality sedation that was associated with quick recovery, hemodynamic evaluation, and sedation-related complications.[14] In a different study showed that a combination of 1mcg/kg fentanyl and 1 mg/kg propofol in cataract surgery provides appropriate sedation and safe anesthesia with lower complications and acceptable satisfaction in patients and surgeons.[20] According to Rewari et al, a minimal dose of opioid and propofol in sedation with a combination of 0.5 mcg/kg remifentanil and 0.5 mg/kg propofol as a bolus in cataract surgery provided excellent relief of pain and anxiety with the fewest adverse effects from ophthalmic block placement.[21] Meanwhile, Ferrari et al reported that the administration of 0.47 mg/kg propofol has other advantages besides being amnestic and anxiolytic. These advantages include its ability to reduce the incidence of nausea and vomiting, decrease intraocular pressure, and fast recovery time.[22] The result from this study showed that the mean dose of fentanyl and propofol was 0.43 mcg/kg and 0.21 mg/kg, respectively. According to Habib et al, the administration of a subanesthetic dose of propofol of 15–75 mg before peribulbar block injection was effective in reducing the patient's memory during the procedure.[23] Meanwhile, the dose range of propofol used in this study was 10–30 mg.

In a previous study, 70 patients over 60 years old with cataract surgery who were given fentanyl and a bolus dose of 25–50 mcg provided analgesia with minimal sedation.[24] The dose range of fentanyl given in this study was 10–50 mcg, which is lower than the previous studies.

Sedation Level

According to ASA guidelines, the preferred sedation level in ophthalmic surgery is either minimal or moderate.[11] Furthermore, Ramsay's sedation score of 2 or 3 is preferable during cataract surgery,[25] because spontaneous ocular movement at this level is common and the procedures are frequently hindered at scores of 4 or 5. Park et al reported that deep sedation in cataract surgery is related to poor patient cooperation and lower surgeon satisfaction.[26] Higher sedation score is also associated with lower recovery time.[14] This study's results showed that the use of a low-dose combination of propofol and fentanyl gives a Ramsay sedation score of 2 or 3 on all patients.

Blood Pressure

Several factors such as systemic absorption of an anesthetic drug, use of intracameral adrenaline for pupillary dilation, patient anxiety, and discomfort such as iris touch causing pain in topical anesthesia can cause blood pressure changes during cataract surgery. Any increase in blood pressure during surgery can lead to ocular and systemic complications such as suprachoroidal hemorrhage, stroke, or myocardial ischemic events. Furthermore, the blood pressure changes in phacoemulsification surgery may require constant monitoring to achieve favorable ocular and systemic outcomes. These changes need to be observed in order to make a timely intervention to

achieve favorable postoperative outcomes. The result of a study conducted by Singh et al on cataract patients comparing topical anesthesia and peribulbar block showed that the increase in intraoperative systolic blood pressure in the topical group is due to the discomfort from microscopic light, iris manipulation, irrigation, and aspiration during surgery. Furthermore, the mean preoperative systolic blood pressure was higher in the topical group, which is probably due to anxiety or stress under topical anesthesia.[15] It is a fundamental necessity to monitor anesthesia care to prevent such complications. The result of a study conducted by Shetabi et al on the use of propofol and fentanyl for cataract surgery found a significant reduction in heart rate, systolic, and diastolic blood pressure.[20] Similarly, Adinnehmer conducted a study on cataract patients found that pulse rate, systolic and diastolic blood pressure, and mean arterial blood pressure decreased significantly in the three groups during the procedure until recovery time ($P < 0.001$).[14] In this study, a significant decrease in systolic blood pressure, diastolic blood pressure, MAP, and heart rate was found after the administration of low-dose propofol and fentanyl ($p < 0.001$).

Side Effects

One study on 19.250 cataract surgeries at nine centers in the United States and Canada from June 1995 through June 1997 showed that the use of intravenous anesthetic agents significantly increases the incidence of the adverse event compared to topical or injection anesthesia.[27] Combined regimens of intravenous sedatives and opioids can decrease the amounts of each drug administered which can reduce the side effects.[7] Another study compared the use of sedation and analgesia using ketamine/propofol combination versus fentanyl/propofol in 60 patients undergoing colonoscopy. The result showed that the incidence of nausea and vomiting was 12.5% in both groups.[28] In this study, the use of combination therapy of fentanyl and propofol at a low dose resulted in 4% pain during cataract surgery, as well as 8% postoperative side and 8% dizziness. No vomiting or nausea was found in all the patients receiving the low-dose anesthesia.

Satisfaction Rate

According to Adinnehmeir, propofol has a superior satisfaction rate compared to midazolam and etomidate, with each patient's satisfaction rate being sequentially 4.88, 4.77, and 4.48, respectively. Furthermore, Aghadavoudi et al[29] and Lee-Jayaram et al[30] compared the efficacy of etomidate-fentanyl versus ketamine midazolam in procedural sedation for cataract surgery and pediatric orthopedic reductions, respectively. Both studies showed that the satisfaction score of patients was significantly higher.

Limitation

Blood pressure was not always evaluated during the surgery, but only during the first five minutes after drug administration due to the surgery length variability.

Conclusion

Based on the data, the combination of 10–30 mg propofol and 10–50 mcg fentanyl can be used in cataract phacoemulsification surgery because it can achieve an ideal Ramsay score, significant reduction in blood pressure, minimal side effects, and acceptable satisfaction rate.

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Disclosure

The authors declare having no conflicts of interest for this article.

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