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A Prospective Evaluation of Different Ketofol Concentrations for Sedation and Analgesia in Catarct Surgery Performed Under Local Anesthesia

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Abstract

Background: Ketofol is a mixture of ketamine and propofol. It is one of the agents known to achieve procedural sedation and analgesia.

Aim of Study: This prospective randomized study compared the effectiveness and safety of four doses of ketofol for sedation and analgesia in catarct surgery performed under local anesthesia.

Patients and Methods: 80 adult patients aged between 40-65 years of both sexes, scheduled for cataract extraction and intraocular lens implantation, were enrolled in this, interventional study. They were divided into 4 groups of 20 patients each.

Results: In the present study as regards to haemodynamics (HR & MAP), we found most patients developed modest increases in pulse rate and blood pressure in all groups but the higher increase was found in groups I & II compared to III & IV. As regards to mean oxygen saturation and respiratory rate in the current study there was lower mean oxygen saturation in groups III and IV after 5 minutes of drug infusion (T1) compared to the other groups. However, the difference is not statistically significant (p-value >0.05). Mean IOP after sedation was significantly higher among groups I & II compared to groups III & IV (p-value <0.05) which is related to the ketamine high doses.

Conclusion: This current study suggests that Ketofol (ketamine/propofol concentration) at a ratio 3:1 and 4:1 may provide effective and safe sedation for patients undergoing ophthalmic procedures under regional anesthesia. An intravenous infusion of a 4:1 ratio is a suitable alternative for delivering ketofol, this provides more stability and consistency of sedation depth and less need for top-up doses that may lead to overshoot of sedation and a delayed recovery.

Key Words: *Ketamine – Propofol – Ketofol – Sedation and analgesia – Catarct surgery performed under local anesthesia.*

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Introduction

CATARACT surgery is the commonest ophthalmic surgical procedure and a local anaesthetic technique is usually preferred. Patient comfort, safety and low complication rates are the essentials of local anaesthesia. The anaesthetic requirements for ophthalmic surgery are dictated by the nature of the proposed surgery, the surgeon's preference and the patient's wishes. The provision of ophthalmic regional anaesthesia for cataract surgery varies worldwide. These may be chosen to eliminate eye movement or not and both non-akinetic and akinetic methods are widely used **[1,2]**.

Some drawbacks are linked with regional anaesthesia techniques: pain at the puncture site, fear of needles, and recall of the procedure. These factors stress the importance of sedation that offers analgesia, anxiolysis, and amnesia. Sedation has been shown to increase patient satisfaction during regional anaesthesia and may be considered as a mean to increase the patient's acceptance of regional anaesthetic techniques **[3]**.

A multitude of sedative and analgesic agents are frequently used. Titration of anesthetic doses should be done cautiously and the patients should be continuously monitored. So far, an ideal intravenous anesthetic agent doesn't exist **[4]**. Ketofol is the combination of ketamine and Propofol in various concentrations and it has several ideal properties. It commonly used for several procedural sedation. Ketamine, a neuroleptic anesthetic agent, works on thalamocortical and limbic N-methyl-D-aspartate (NMDA) receptors **[5]**. Ketamine stimulates the cardiorespiratory system. A direct effect increases cardiac output, arterial blood pressure, heart rate and central venous pressures. Therefore,

it is a valuable agent for hypotensive or hypovolemic patients, but a less desirable agent in patients with ischemic heart disease or raised pulmonary vascular pressure. Ketamine induces psychomimetic activity and emergence reactions in up to 30% of patients. In contrast, propofol, a sedative, hypnotic and anesthetic agent, is also an antagonist at N-methyl-D-aspartate receptors [4]. However, propofol has a narrow therapeutic range and risks of cardiovascular depression [5].

Combining these two agents; preserve sedation efficacy while minimizing their adverse effects; thus, theoretically balance each other out when used together.

Aim of the work:

A number of studies have demonstrated that the combination of ketamine and propofol (Ketofol) for sedation is safe and effective in different concentration. We compare the safety and efficacy of 4 concentrations of ketofol; group I ketofol in 1:1 ratio, group II 2:1, group III 3:1 and group IV ketofol in 4:1 ratio, given in bolus dose before the needle-based eye block and infusion through the operation.

Patients and Methods

This prospective study was conducted in the Anaesthesia Department of The Eye Hospital at Alexandria from 27th January 2020 to 15th October 2020. After proper discussion with the patient regarding the nature of anesthetics and sedation procedure, informed consent was obtained.

Sampling method: Eighty adult patients aged between 40-65 years of both sexes, graded as ASA physical status I-III, scheduled for cataract extraction and intraocular lens implantation on an ambulatory surgery basis, were enrolled in this, prospective randomized double-blinded clinical trial. They were divided into 4 groups of 20 patients each, utilizing a computerized random number table. Concealment was done by sealed opaque envelope method.

A detailed history was taken including full name, age, medical history, any given medications, surgical history including any past operation and type of anesthesia given. Any complications related to previous anesthetic techniques or allergy to any medication was recorded. The anesthetic and surgical procedures were explained to the patients to enable informed consent.

Upon arrival to the operating theatre, intravenous cannula was inserted and standard monitors were attached to the patients. A proper backup for general anesthesia was prepared and emergency drugs were drawn up.

Sample size: A sample size of 20 patients for each group will achieve more than 90% power to detect a difference in pulse rate of about (5bpm) between groups using PASS 11 program for sample size calculation.

Inclusion criteria: 80 adult patients aged between 40-65 years of both sexes, graded as ASA physical status I-III.

Exclusion criteria:

- Patients with BMI >35kg/m.
- Uncontrolled hypertension (systolic/diastolic >170/100mmHg) and sever cardiovascular disease.
- History of allergy to ketamine, propofol or local anesthetic drugs.
- Patients receiving any psychotropic medications or those with dementia, deafness, movement disorders or hyperanxiety.
- Patients on anticoagulants with INR over 1.3.
- Patients with hepatic disease, renal disease, seizure disorders, pregnancy, increased intracranial pressure and glaucoma are also excluded.

Study procedure: The study drug for patients in the Group I ketofol (1:1) admixture; was prepared in a 50ml syringe by mixing 1 0ml propofol 1% (10mg/ml) with 2ml ketamine (50mg/ml) and 38ml saline so that the propofol concentration will be 2mg/ml and ketamine 2mg/ml.

Group II ketofol (2:1) admixture; was prepared by mixing 20ml propofol 1% (10mg/ml) with 2ml ketamine (50mg/ml) and 28ml saline, so that the propofol concentration is 4mg/ml and ketamine 2mg/ml.

Group III ketofol (3:1) was prepared by mixing 30ml propofol 1% (10mg/ml) with 2ml ketamine (50mg/ml) and 18ml saline so that the propofol concentration will be 6mg/ml and ketamine 2mg/ml.

Group IV ketofol (4:1) was prepared by mixing 40ml propofol 1% (10mg/ml) with 2ml ketamine (50mg/ml) and 8ml saline so that the propofol concentration will be 8mg/ml and ketamine 2mg/ml. The patients and surgeons were blind to the technique of sedation and analgesia used in this study.

The study drug preparation:

P:K ratio in groups	Propofol 1% (10mg/ml)	Ketamine 5% (50mg/ml)	Saline (50ml syringe)	Conc. of P in Ketofol mixture (mg/ml)	Conc. of K in Ketofol mixture (mg/ml)
I=1:1	100mg (10ml)	100mg (2ml)	38ml	2mg/ml	2mg/ml
II=2:1	200mg (20ml)	100mg (2ml)	28ml	4mg/ml	2mg/ml
III=3:1	300mg (30ml)	100mg (2ml)	18ml	6mg/ml	2mg/ml
IV=4:1	400mg (40ml)	100mg (2ml)	8ml	8mg/ml	2mg/ml

Measurements:

Cardiopulmonary changes:

1- Baseline mean arterial pressure (MAP) and heart rate (HR) was recorded before sedation and after injection of the study drug, then every 5min for the duration of surgery, then at 5, 10 and 15min postoperative. Intervention for hemodynamic changes will be noted.

2- Degree of respiratory depression and airway patency was evaluated by monitoring oxygen saturation (SpO2) and respiratory rate.

Intraocular pressure:

IOP was measured before the administration of the study drug and after the administration of the study drug (after the assessment of the block efficiency).

Sedation characteristics:

1- Hypnotic dose and supplemental dose of the study drug were recorded.

2- Quality of sedation at the hypnotic level:

2=No movement or grimacing by the patient during needle insertion; 1=Grimacing and minimal movement of upper extremities; 0=Grimacing and upper extremity movement requiring restraining and administration of supplemental study drug [7].

3- The time to achieve adequate sedation level using the modified assessment of alertness and sedation score 4 (Lethargic response to name spoken in normal tone).

Recovery characteristics:

1- Recovery time: The time from the end of drug delivery until home discharge from PACU.

2- Adverse events including, but not limited to nausea, vomiting, dizziness, confusion, agitation, respiratory depression (RR <10 BPM) or oxygen desaturation (Spo2, 92%) were recorded.

Patient and surgeon satisfaction:

After recovery, patients were asked to answer the question “How would you rate your experience during surgery?” using a 7-point Likert-like verbal rating scale; 1-extremly dissatisfied, 2-dissatisfied, 3-somewhat dissatisfied, 4-undecided, 5-somewhat satisfied, 6-satisfied, 7-extremely satisfied [6].

1	2	3	4	5	6	7
Extremely dissatisfied	Dissatisfied	Somewhat dissatisfied	Undecided	Somewhat satisfied	Satisfied	Extremely satisfied

The surgeon was asked to rate his satisfaction with the patient sedation using the same method and scale at the end of surgery.

Outcomes:

Primary outcome was the effect of different ketofol concentrations on cardiopulmonary changes, intraocular pressure and recovery characteristics.

Secondary outcome was recording the optimum dose of ketofol needed for achieving a rapid onset of sedation-analgesia, the shortest emergence time, and antiemetic effect.

Statistical analysis: Recorded data were analyzed using the statistical package for social sciences, version 24.0 (SPSS Inc, Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as count and percentage.

The following tests were done: One way ANOVA test was used to compare quantitative data between different groups followed by Bonferroni pairwise comparison for significant results. Paired samples *t*-test and Repeated measures ANOVA test were used to compare quantitative data for the same group at different time points (with between subject factor analysis). Chi square test was used to compare qualitative data between different groups.

Probability (p-value): *p*-value <0.05 was considered significant, *p*-value <0.001 was considered as highly significant and *p*-value >0.05 was considered insignificant.

Results

Table (1): Demographic data in the study groups presented as Mean ± standard deviation (SD) and frequency (%).

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Age	52.00	4.90	52.30	5.91	53.75	5.56	54.10	6.66	0.65	0.59 NS
	N	%	N	%	N	%	N	%	x^{2**}	*p*-value
Gender:										
Male	16	80.0%	9	45.0%	12	60.0%	11	55.0%	5.42	0.14 NS
Female	4	20.0%	11	55.0%	8	40.0%	9	45.0%		
BMI	23.35	2.54	22.25	2.40	23.35	2.54	22.25	2.40	1.32	0.27 NS
	N	%	N	%	N	%	N	%	x^{2**}	*p*-value
ASA:										
I	10	50.0%	11	55.0%	7	35.0%	11	55.0%	3.55	0.80 NS
II	9	45.0%	8	40.0%	12	60.0%	9	45.0%	FE	
III	1	5.0%	1	5.0%	1	5.0%	0	0.0%		
ASA:										
I	10	50.0%	11	55.0%	7	35.0%	11	55.0%	2.15	0.54 NS
II/III	10	50.0%	9	45.0%	13	65.0%	9	45.0%		
HTN:										
Yes	7	35.0%	6	30.0%	7	35.0%	9	45.0%	1.03	0.80 NS
No	13	65.0%	14	70.0%	13	65.0%	11	55.0%		
DM:										
Yes	5	25.0%	5	25.0%	5	25.0%	2	10.0%	2.18	0.56 NS
No	15	75.0%	15	75.0%	15	75.0%	18	90.0%	FE	
BA:										
Yes	4	20.0%	2	10.0%	3	15.0%	2	10.0%	1.21	0.89 NS
No	16	80.0%	18	90.0%	17	85.0%	18	90.0%	FE	
RA:										
Yes	0	0.0%	2	10.0%	2	10.0%	1	5.0%	2.41	0.75 NS
No	20	100%	18	90.0%	18	90.0%	19	95.0%	FE	

*One way ANOVA test. **Chi square test (FE: Fisher Exact).

Table (2): Cardiopulmonary measures at baseline time (T0).

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
HR (T0)	71.80**a**	8.13	77.1 0**b**	5.20	77. 10**b**	7.23	75.30	6.19	2.718	0.050 S
MAP (T0)	94.60**a**	9.46	95.40	7.24	95.40	8.98	101.80**b**	10.66	2.680	0.053 NS
O2. saturation (T0)	98.00	0.97	98.00	1.34	97.25	1.12	97.35	1.31	2.316	0.082 NS
RR (T0)	13.30	1.69	13.20	1.28	12.65	1.31	12.45	1.10	1.852	0.145 NS

*One way ANOVA test (**a, b, c**: Bonferroni post hoc test). *T0: Baseline time before drug infusion.

Table (3): Cardiopulmonary measures after 5 minutes of drug infusion (T1).

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
HR (T1)	82.60**a**	7.34	80.20	5.38	78.00	7.42	76.20**b**	6.39	3.433	0.021 S
MAP (T1)	108.10**a**	9.64	104.80**a**	7.24	93.20**b**	8.97	95.30**b**	10.46	12.450	<0.001 HS
O2. saturation (T1)	97.00	1.03	97.00	1.21	96.30	.86	96.60	.94	2.229	0.092 NS
RR (T1)	14.20**a**	1.54	13.15	1.66	12.20**b**	1.36	12.25b	1.12	8.585	<0.001 HS

*One way ANOVA test (**a, b, c**: Bonferroni post hoc test). *T1: 5 minutes after drug infusion.

HR (T2)	76.40**a**	6.44	82.00**b**	5.03	77.60	7.13	74.70**b**	6.38	4.917	0.004 HS
MAP (T2)	101.60**a**	8.73	99.60**a**	7.36	93.10**b**	8.84	91.80**b**	10.24	5.894	0.001 HS
O2. saturation (T2)	97.00	.79	97.45	1.64	97.15	1.31	97.10	1.33	.441	0.724 NS
RR (T2)	12.30	1.56	12.45	1.47	12.15	.88	12.15	.81	.274	0.844 NS

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
HR (T3)	74.60**a**	6.81	82.40**b**	4.69	77.70	7.07	75.40**a**	6.37	6.184	0.001 HS
MAP (T3)	100.80**a**	7.95	99.30**a**	7.79	94.20	9.88	87.80**b**	9.61	8.800	<0.001 HS
O2. saturation (T3)	97.75	1.12	98.10	1.25	97.80	1.44	98.00	1.30	.333	0.802 NS
RR (T3)	12.50	1.36	13.40	1.39	13.00	.97	13.05	.69	2.113	0.106 NS

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
HR (T4)	81.20	6.59	83.40**a**	4.43	77.50**b**	7.15	79.20	6.49	3.321	0.024 S
MAP (T4)	99.30**a**	7.54	100.10**a**	6.42	95.00**a**	8.72	85.30**b**	9.35	14.126	<0.001 HS
O2. saturation (T4)	99.00	1.03	98.00	1.41	98.15	1.39	98.25	1.37	2.314	0.083 NS
RR (T4)	12.45	1.39	13.35	1.42	13.10	.85	13.00	.73	2.207	0.094 NS

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
HR (T5)	83.20**a**	6.08	88.50**b**	4.27	78.50**a**	7.18	78.80**a**	7.11	11.178	<0.001 HS
MAP (T5)	94.50**a**	6.53	97.80**a**	6.11	95.10**a**	8.87	81.30**b**	9.19	17.970	<0.001 HS
O2. saturation (T5)	98.10	1.17	98.30	.86	98.10	1.17	98.15	1.18	.147	0.931 NS
RR (T5)	12.35	1.27	13.10	1.45	13.15	.81	12.95	.83	2.151	0.101 NS

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
IOP. Before	15.00	2.97	15.40	2.84	13.60	1.57	14.90	2.25	2.00	0.12 NS
IOP. After	17.00**a**	2.73	16.20**a**	2.91	13.40**b**	2.06	14.20**b**	2.09	9.20	<0.001 HS

*One way ANOVA test (**a, b, c**: Bonferroni post hoc test).

Table (9): Sedation characteristics.

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Time to achieve score 4 MOAAS	8.40**a**	1.23	6.70**b**	1.49	3.60**c**	1.23	1.30**d**	.59	143.20	<0.001 HS
Total p dose	133.40	6.88	127.00	7.88	127.15	7.80	126.80	13.86	2.28	0.09 NS
Total k dose	133.40**a**	6.88	63.50**b**	3.94	42.35**c**	2.52	31.70**d**	3.47	2060.35	<0.001 HS
Infusion duration	54.00**a**	4.21	46.20**b**	3.58	45.60**b**	2.60	42.60**b**	4.25	34.20	<0.001 HS
	N	%	N	%	N	%	N	%	x^{2**}	*p*-value
Quality of sedation:										
Grade I	19	95.0%	14	70.0%	3	15.0%	2	10.0%	41.91	<0.001 HS
Grade II	1	5.0%	6	30.0%	17	85.0%	18	90.0%		

*One way ANOVA test (**a, b, c, d**: Bonferroni post hoc test). **Chi square test (FE: Fisher Exact).

Table (10): Recovery characteristics and Adverse events.

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Recovery time	17.00**a**	2.00	16.00**a**	2.22	14.00**b**	2.47	8.00**b**	2.03	67.86	<0.001 HS
	N	%	N	%	N	%	N	%	x^{2**}	*p*-value
Adverse events:										
Yes	14	70.0%	7	35.0%	3	15.0%	1	5.0%	22.98	<0.001 HS
No	6	30.0%	13	65.0%	17	85.0%	19	95.0%		
Hallucination:										
Yes	8	40.0%	6	30.0%	2	10.0%	0	0.0%	12.94	0.004 HS
No	12	60.0%	14	70.0%	18	90.0%	20	100%	FE	
Nausea:										
Yes	5	25.0%	3	15.0%	1	5.0%	0	0.0%	6.77	0.01 HS
No	15	75.0%	17	85.0%	19	95.0%	20	100%	FE	
Vomiting:										
Yes	5	25.0%	1	5.0%	0	0.0%	0	0.0%	8.64	0.01 HS
No	15	75.0%	19	95.0%	20	100%	20	100%	FE	
Snoring:										
Yes	0	0.0%	0	0.0%	2	10.0%	1	5.0%	3.00	0.61 NS
No	20	100%	20	100%	18	90.0%	19	95.0%	FE	
Dizziness:										
Yes	2	10.0%	1	5.0%	0	0.0%	0	0.0%	3.00	0.61 NS
No	18	90.0%	19	95.0%	20	100%	20	100%	FE	
Airway malaligment:										
Yes	0	0.0%	0	0.0%	1	5.0%	1	5.0%	2.16	1.00 NS
No	20	100%	20	100%	19	95.0%	19	95.0%	FE	

*One way ANOVA test (**a, b, c**: Bonferroni post hoc test). **Chi square test (FE: Fisher Exact).

Table (11): Surgeon and patient satisfaction.

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Group IV (N=20)		F*	*p*-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Surgeon satisfaction	2.60**a**	1.05	3.00**a**	1.21	5.30**b**	1.26	5.95**b**	0.60	48.76	<0.001 HS
Patient satisfaction	3.45**a**	1.39	4.35**a**	1.23	5.00**b**	1.12	5.50**b**	0.83	11.63	<0.001 HS

*One way ANOVA test (**a, b, c**: Bonferroni post hoc test).

Discussion

In the present study as regards to haemodynamics (HR & MAP), we found most patients developed modest increases in pulse rate and blood pressure in all groups but the higher increase was found in groups I & II compared to III & IV.

After 5 minutes of drug infusion(T1), there was significant difference in heart rate at (T1) between group I and group IV (p-value=0.021). Additionally, there is also significant difference in mean blood pressure between group I,II and group III,IV.

Hemodynamic depression was not encountered in any of the 4 studied groups. Our results are consistent with Andolfatto et al., [8], who evaluated the effectiveness and safety of Ketofol 1:1 mixture (ketamine 1 0mg & propofol 1 0mg) in a prospective case series of 114 patients for procedural sedation and analgesia in the ER, they reported modest increase in HR and BP without any incidence of hypotension or signs of poor perfusion.

As regards to mean oxygen saturation and respiratory rate in the current study there was lower mean oxygen saturation in groups III and IV after 5 minutes of drug infusion (T1) compared to the other groups. However, the difference is not statistically significant (p-value >0.05), which coincides with Akin et al, who compared propofol to propofol plus ketamine 3:1 in 60 patients undergoing auditory brainstem response testing and concluded that the addition of low dose ketamine to propofol reduced the risk of respiratory depression [9].

Significant increases in IOP have been reported with ketamine using indentation tonometry. We used the more sensitive applanation to nometry technique; a decrease of IOP was noted in group III and IV which can be explained by the higher dose of propofol in these 2 groups. Mean IOP after sedation was significantly higher among groups I & II compared to groups III & IV (p-value <0.05) which is related to the ketamine high doses. This goes in line with Kere Frey et al., who compared the sedation quality, IOP changes and recovery profiles in 70 elderly patients who received propofol or ketofol sedation during placement of retrobulbar block; they found a consistent decrease in IOP in both groups [7].

In the current study, the mean time to achieve MOAA/S 4 was 8.4min in group I which is the highest with significant difference with all the studied groups. This was related to the deeper level of sedation achieved in group I after the bolus dose (0.5mg/kg).

More patients in groups III (3:1) 85% and IV (4:1) 90% had grade 2 (no movement or grimacing) quality of sedation at bolus dose compared to group II (2:1) 30% during needle insertion for peribulbar block. This coincides with Santiveri et al., who studied the quality of sedation with ketofol and compared it with propofol; they concluded that puncture conditions were significantly better in the ketamine plus propofol group [10].

However, 95% patients in group I experienced grimacing and minimal movement of upper extremities (grade 1) during needle insertion. This may be explained by the oversedation that occurred after bolus dose which exposed patients to the risk complications during eye block in this group.

In the current study, mean recovery time of 17 ±2 minutes reported in groups I (1:1) and of 16 ±2.22 minutes in group II (2:1) is comparable to that previously reported in literature. Willman and Andolfatto evaluated the effectiveness of ketofol 1:1 for procedural sedation and analgesia on emergency department, and reported median recovery time of 15 minutes [11]. However, Erden et al., reported 12 ± 1 minutes with ketofol 1:1 and 13.8±0.8 minutes with ketofol 2:1 ratio [12].

In this study the mean recovery time in group III (3:1) was 14 ± 2.47 minutes; however time to discharge was longer in groups I and II, secondary to the increased presence of adverse events, leading to a longer time until discharge. The shortest mean recovery time in this study was 8 ± 2.03 minutes in group IV (4:1), which goes in hand with Daabiss et al, who used the same ketofol ratio 4:1 in procedural sedation and analgesia and reported mean recovery time of 8.2 ± 6.7 minutes [13].

In this study, adverse events with ketofol 1:1 ratio in group I was highly significant compared to the other groups. Adverse events include; unpleasant emergence reactions manifested as hallucination and agitation in 40% of patients, which resolved promptly after intravenous midazolam. Vomiting was reported in 25% of patients and managed with 5HT3 antagonist granisetron 0.1mg/kg. Emergence reactions and vomiting are considered to be significant adverse effects of ketamine usage, occurring more often in adults than children. In a study by Green et al., [14] emesis was reported in 6.7%, mild emergence in 17.6%, and moderate to severe agitation in 1.6% of patients. Chudnofsky et al., described emergence phenomena in up to 50% of adults [15].

In the current study results coincides with Frey et al., who compared the sedation quality, IOP

changes and recovery profiles of propofol versus ketofol in 70 elderly patients performing retrobulbar block, they reported 12% of patients in ketofol group had a brief episode of coughing after retrobulbar block **[7]**.

The mean satisfaction scores were high in the current study for both patients and surgeons in group III 3:1 and group IV 4:1 where very few adverse events occurred and more consistent depth of sedation was maintained through the procedure, while very low satisfaction scores were reported in groups I (1:1) & II (2:1) which is comparable to results described in literature. Akin et al., in a trial of 40 adult patients undergoing endometrial biopsy, compared the combination of propofol plus fentanyl to the combination of ketofol 2:1, they concluded that the increased presence of adverse events including nausea, vertigo, and visual disturbances lead to a longer time until discharge and had a lower overall patient satisfaction **[16]**.

Conclusion:

This current study suggests that Ketofol (ketamine/propofol concentration) at a ratio 3:1 and 4:1 may provide effective and safe sedation for patients undergoing ophthalmic procedures under regional anesthesia. An intravenous infusion of a 4:1 ratio is a suitable alternative for delivering ketofol, this provides more stability and consistency of sedation depth and less need for top-up doses that may lead to overshoot of sedation and a delayed recovery.

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دراسة مستقبلية لتقييم جرعات ذات تركيز مختلف من خليط البروبوفول والكيتامين للتهدئة وتسكين الآلام فى عمليات الرمد تحت تأثير مخدر موضعى

يعتبر عقار الكيتوفول أحد المركبات المفيدة مهدئ فى عمليات العيون التى تجرى بواسطة التخدير الموضعى غير أنه يجب متابعة العلامات الحيوية للمريض بدقة ويجب اختيار نسبة العقارات بعناية. هذا ويتعين اتخاذ القرار ما إذا كانت هذه النسبة أنسب لإعطاءه كجرعة واحدة يليها جرعات متقطعة أو حقن متواصل للعقار.

نستطيع القول من جميع الدراسات السابقة أن هناك مميزات محتملة عند استخدام الكيتوفول وعندما يكون الهدف هو تهدئة المريض بدرجة متوسطة وتسكين الألم:

- يمكن استخدام جرعات أقل من البروبوفول وبهذا يقل هبوط التنفس المصاحب للبروبوفول.
- توفير المسكنات من خلال الكيتامين دون الهبوط التنفسى الذى عادة ما نراه عند إعطاء المسكنات الأفيونية.
- وقت أقصر محتمل للإفاقة واحتمالية أقل حدوث الغثيان والقئ وظاهرة الإفاقة ما بعد العملية اعتماداً على نسبة الكيتا ميتوال بروبوفول المستعملة فى الخليط.

تعتبر النسبة ١:٣ (كيتامين بروبوفول) هى المناسبة لإعطاء الجرعة محققة بداية سريعة للتهدئة ولتسكين الألم، و قت أقل للإفاقة والتأثير ضد القئ، وبنسب أعلى يطول وقت الإفاقة. بالإضافة إلى ذلك وبسبب الجرعات الأعلى من الكيتامين فإن احتمالية ظاهرة الإفاقة والقئ من الممكن أن تتزايد. وفى النسب الأقل يصبح وقت الإفاقة أسرع وتتحسن جودة التهدئة وتصبح الآثار الجانبية أقل.

أما النسبة ١:٤ للحقن المتواصل فيبدو أنها أفضل لأن الجرعة الكلية لكلا العقارين المطلوبة للوصول لنفس التأثير النهائى عملياً أقل مع الحقن الثابت، ولذا فعنصر الكيتامين المسؤول عن وقت إفاقة أطول بكثير من الممكن أن يخفض وبالتالى يتم تحقيق مستوى ثابت من التنويم.

تقترح هذه الدراسة أن الكيتوفول (كيتامين/بروبوفول) بنسبة ١:٣ و ١:٤ قد يوفر التهدئة العفالة والآمنة لمرضى عمليات العيون المجراة تحت تأثير المخدر الموضعى. ويعتبر الحقن من خلال الوريد بنسبة بديلا مناسباً لإعطاء الكيتوفول موفراً استقرار أو ثباتاً أكبر فى مستوى التهدئة واحتياج أقل إلى الجرعات المتتابعة التى قد تؤدى إلى المبالغة فى التنويم والتأخر فى الإفاقة.

\التوصيات: مزيد من التجارب العشوائية المعايرة عن استخدام الكيتوفول بالحقن بنسبة ١:٤ كنظام للتهدئة لعمليات العيون المطولة المجربة بتخدير موضعى مازالت مطلوبة لتدعيم هذه النتيجة.