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A clinical, comparative, prospective, and observational study of two different ratios of ketamine and propofol in short surgical procedures at a tertiary care hospital

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ABSTRACT

Background: Ketamine and propofol are two medications commonly used for procedural sedation because they possess many of the desired characteristics including rapid induction and recovery. The opposing physiologic effects of ketamine and propofol suggest the potential for synergy, and this has led to an interest in their combined use, commonly termed "Ketofol." The purpose of this study is to compare two different proportions of ketamine and propofol, 1:2 and 1:3 in short surgical procedures. **Aims and Objectives:** The aim of the study was to compare the quality of analgesia, level of sedation, and respiratory and hemodynamic parameters of two different proportions of ketamine and propofol in the ratio of 1:2 and 1:3 in short surgical procedures. **Materials and Methods:** After obtaining approval from the institutional ethics and scientific committee, with IEC no.MIMS/IEC/2021/474 dated February 23, 2021, 86 consenting patients of 18–60 years categorized under American Society of Anesthesiologists Category I and II undergoing elective short surgical procedures lasting for about 20 min were selected. The study patients were divided into two groups of 43 each by convenient sampling method. In Group A, 43 patients received 1 mL of ketamine (50 mg/mL) mixed with 10 mL of 100 mg propofol (10 mg/mL). In Group B, 43 patients received 30 mg of ketamine mixed with 9 mL of 90 mg propofol (10 mg/mL). Non-invasive blood pressure, heart rate, oxygen saturation, Ramsay Sedation Score, Modified Aldrete Score, and any incidence of side effects were recorded. **Results:** The quality of analgesia and level of sedation was achieved better in Group A compared to Group B. No significant difference was observed between the two groups with respect to hemodynamic and respiratory parameters. **Conclusion:** The combination of propofol and ketamine has several benefits such as hemodynamic stability, lack of respiratory depression, good recovery, and potent procedural analgesia. Ketofol 1:2 proportion is comparatively better and can be used safely in short surgical procedures.

Key words: Ketamine; Procedural sedation; Propofol

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INTRODUCTION

Procedural sedation defines as "a technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function.[1,2] Procedural sedation and analgesia (PSA) is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently." According to the American Society of Anesthesiologists (ASA) guidelines, most procedural sedation falls within the level of moderate sedation/analgesia although very painful procedures may require deep sedation/analgesia.[3]

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Ketamine is a unique agent in PSA in that it is a "dissociative" anesthetic. It is unique in that the patient appears awake but is detached from the surroundings with eyes remaining open.[4] Ketamine is a sedative and analgesic drug that can be used for analgesia alone or with others drugs. Ketamine was the only safe and effective anesthetic drug that has rare limitations such as delayed recovery, nausea, and vomiting. Ketamine does not cause the respiratory depression but it raises the blood pressure and heartbeat with sympathetic stimulation.[5]

Propofol is a short-acting, sedative, intravenous, and anesthetic drug that is used in the induction and maintenance of anesthesia in adults and children.[5] It also has the advantages of functioning as an antiemetic, anticonvulsant, and amnestic agent. Although extremely effective and potent, propofol use is limited by a relatively increased incidence of dose-dependent hypotension and respiratory depression.[3] It has been found to PSA in gynecologic, ophthalmologic, orthopedic, and cardiovascular procedures in all age groups.[6,7]

It is postulated that combining these two agents for PSA may preserve sedation efficacy while minimizing their respective adverse effects.[8-10] This is due partly to the fact that many of the potential adverse effects are dose-dependent and when used in combination the doses administered of each can be reduced.[11-13] Furthermore, the cardiovascular effects of each are opposing in action, thus theoretically balancing each other out when used together.[3,12,14]

Ketofol has a fast onset and good analgesic and sedative properties, thus making it ideal for short surgical procedures.[12,14] Studies using 1:1 and 1:2 proportions of ketofol are common. A 1:1 ratio of ketofol caused more sedation and delayed recovery.[12,15,16] Hence, we were designed to compare the quality of analgesia and level of sedation and hemodynamic parameters between two different proportions of ketofol, that is, 1:2 and 1:3 in short surgical procedures.

Aims and objectives

To compare the quality of analgesia, level of sedation and hemodynamic parameters between two different proportions of ketofol.

MATERIALS AND METHODS

After obtaining approval from the institutional ethics committee and institutional scientific committee, with IEC no. MIMS/IEC/2021/474 dated February 23, 2021, 86 consenting patients of 18–60 years categorized under ASA Category I and II undergoing elective short surgical procedures lasting for about 20 min were included for this prospective, comparative, and observational study. Pregnant women, patients on chronic drug abuse, allergic to eggs, and with psychiatric disorders were excluded from the study.

Patients were divided into two groups of 43 each, by convenient sampling method. In Group A, 43 patients who received 50 mg of ketamine mixed with 10 mL of 100 mg propofol (10 mg/mL) and such that each mL contains 4.5 mg ketamine and 9 mg propofol, that is, 1:2 ratios were included in the study. Group B, 43 patients who received 30 mg of ketamine mixed with 9 mL of 90 mg propofol (10 mg/mL) such that each mL contains 3.3 mg of ketamine and 9.9 mg of propofol 1:3 ratios.

The parameters assessed are:

1. Onset of induction: loss of verbal contact
2. Time to sedation was recorded as time from the starting dose till a Ramsay Sedation Score (RSS) of 5 was achieved
3. Non-invasive blood pressure, heart rate, and oxygen saturation (SPO_2) were recorded before sedation, then every 5 min during the procedure till 15 min after the end of the procedure
4. RSS was measured every 5 min during the procedure. The goal was to be to maintain a RSS of 5 with no limb movement and/no patient grimacing (Table 1)
5. Duration of procedure was noted from local anesthesia infiltration with 10 mL of injection lidocaine with adrenaline at the surgery site till the last skin stitch
6. A maximum dose of 0.25 mL/kg of study drug solution was allowed
7. In case of failed sedation (defined as failure to achieve the desired level of sedation), the patients were administered with general anesthesia. Such cases were considered dropouts
8. The maximum duration of surgery was 20 min and cases that required more than 20 min or an extension of incision were considered dropouts
9. Recovery time was recorded as the time taken from the administration of the last dose of the study drug to achieve a Modified Aldrete Score (MAS) of 9 when the patient can be transferred to recovery room (Table 2)
10. Rescue analgesic injection Fentanyl i.v. 0.5–1 mcg/Kg Wt, if given in the intraoperative period is noted
11. Injection diclofenac 75 mg i.v. or injection ketorolac 30 mg i.v. is given as a post-operative analgesic.

Recovery scale-modified Aldrete scale

Aldrete scale is a simple numeric scale for discharge of a patient with points of 9 or 10 measured at the end of anesthesia and 1 h into the post-operative period.

Statistical methods

All the collected data will be entered into Microsoft Excel and data will be analyzed using the Statistical Package for the Social Sciences software. Descriptive statistics such as percentage, mean, standard deviation, range, and correlation to know the relation in the level of sedation between ketofol groups 1:2 and 1:3, and t-test to know the difference between means of two groups of ketofol 1:2 and 1:3 at different point of time. The significance level will be considered at 5% ($P<0.05$).

Table 1: Ramsay Sedation Scale

Score	Conscious level
1	Restless and agitated
2	Cooperative, calm, and oriented
3	Asleep, responds to verbal command
4	Asleep, responds to glabellar tap
5	Asleep, responds sluggishly to glabellar tap
6	No response

Table 2: Modified Aldrete Scale

Characteristics	Score
Activity	
Moves 4 extremities voluntarily or on command	2
Moves 2 extremities voluntarily or on command	1
Unable to move any extremities	0
Arterial oxygenation	
Maintains SaO_2>92% on room air	2
O_2 needed maintain O_2 saturation >90%	1
O_2 saturation <90% even with O_2 supplement	0
Circulation	
Blood pressure <20% of pre-anesthetic level	2
Blood pressure 20–49% of pre-anesthetic level	1
Blood pressure >50% of pre-anesthetic level	0
Conscience	
Fully awake	2
Arousable on calling	1
Not responding	0
Respiration	
Able to deep breath and cough freely	2
Dyspnea or limited breathing	1
Apnea	0

RESULTS

The study groups were comparable with respect to age, ASA physical status**,** heart rate, systolic blood pressure, diastolic blood pressure, and SPO_2.

The mean RSS in Group A at the 5th min is 5.47±0.50, 10th min is 4.63±0.49, 15th min is 4±0.22, and 20th min is 3.70±0.46. The mean RSS in Group B at the 5th min is 4.44±0.40, 10th min is 3.65±0.57, 15th min is 3.21±0.41, and 20th min is 3.05±0.30. Significantly higher RSS s were observed in Group A than in Group B (Table 3).

The mean MAS of 43 patients in Group A is 9.8±0.43 and in Group B is 9.4±0.50. Both groups were comparable in recovery scores (Table 4).

In Group A, none of the patients required rescue analgesic. In Group B, six patients required rescue analgesic ($P=0.026$) (Table 5).

DISCUSSION

The combination of ketamine and propofol for PSA has shown; range of 1:10–1:1 ketamine: propofol can be used depending on the patients' characteristics. The doses required using the combination of the drugs are less than the dose of the individual drugs required to obtain the required level of sedation and the combined drug had a lower frequency of adverse effect in patients undergoing PSA compared to the individual drugs.[17-19]

In the present study, the RSS score was used in the present study as it is simple and easy to use. The mean RSSs were higher and better maintained in patients in Group A (ketofol 1:2) who received a higher amount of propofol intraoperatively compared to the patients in the other group. The outcome of our study is also supported

Table 3: Changes in the Ramsay Sedation Score in both groups

Group	n	Mean	SD	Standard error mean	t-value	Df	P-value*	95% confidence interval of the difference	
								Lower	Upper
RSS 5 min									
Group A	43	5.47	0.50	0.08	9.422	84	<0.001	0.807	1.239
Group B	43	4.44	0.50	0.08					
RSS 10 min									
Group A	43	4.63	0.49	0.07	8.506	84	<0.001	0.748	1.205
Group B	43	3.65	0.57	0.09					
RSS 15 min									
Group A	43	4.00	0.22	0.03	11.129	84	<0.001	0.649	0.932
Group B	43	3.21	0.41	0.06					
RSS 20 min									
Group A	43	3.70	0.46	0.07	7.682	84	<0.001	0.483	0.820
Group B	43	3.05	0.30	0.05					

Table 4: Changes in the Modified Aldrete Score in both groups

Group	n	Mean	Standard deviation	Standard error mean	t-value	Df	P-value*	95% confidence interval of the difference	
								Lower	Upper
Modified Alderete Score									
Group A	43	9.8	0.43	0.07	3.481	84	0.001	0.150	0.548
Group B	43	9.4	0.50	0.08					

Table 5: Rescue analgesic

Group	Rescue analgesic		Total	P-value*
	No	Yes		
Group A	43	0	43	0.026
Group B	37	6	43	
Total	80	6	86	

by the results of other studies Kudri and Deva conclude that ketofol in a ratio of 1:2 provides better sedation level compared to the other groups, both ketofol ratios (1:1 and 1:2) were similar in terms of providing hemodynamic and respiratory stability and producing adverse effects.[8] Wang et al., concluded that ketofol 2:1 had higher sedation in patients undergoing termination of pregnancy.[1]

In our study, there was no statistically significant difference between the two groups at induction, after 5, 10, 15, and 20 min of induction, at the end of the procedure with respect to HR, SBP, and DBP. There was no episode of hypotension or bradycardia in the two groups. Many authors have shown similar results in their studies and found improved cardiovascular stability when using different mixtures of ketamine and propofol in comparison to either drug used alone.[16-18,20] There were no cases of oxygen desaturation in the present study.

No significant difference was observed between groups with respect to recovery scores in our study. Shah et al., concluded that for pediatric orthopedic reductions, the combination of ketamine and propofol in the ratio 1:1 produced slightly faster recoveries.[11] Similar findings were observed in the study conducted by Nalini et al., in patients undergoing puerperal sterilization.[21] Many other studies which evaluated the ketofol in the different ratios for general anesthesia in pediatric patients and concluded that the mixing ratio greater than 1:3 resulted in prolong of recovery.[15,16,20]

In our study, we did not observe any significant adverse effects in the intraoperative or post-operative period. Nonetheless, some other authors have reported less adverse effects of ketofol when compared to propofol alone. The possible explanation for this could be that the addition of ketamine to propofol provides an analgesic component and counterbalances the hemodynamic instability that can be caused by propofol alone. Ketamine also decreases the total dose of propofol needed for the same level of sedation. Moreover, propofol decreases the occurrence of post-operative emergence phenomena associated with ketamine use.

Limitations of the study

Study on larger group of patients would have helped for generalisation of results.

CONCLUSION

We found that ketofol 1:2 provided better RSSs than ketofol 1:3. However, both ketofol ratios (1:2 and 1:3) were similar in terms of providing hemodynamic and respiratory stability. No significant difference was observed between groups with respect to recovery scores in our study. We did not observe any significant adverse effects in the intraoperative or post-operative period. Ketofol (1:2 and 1:3) can be used for short surgical procedures safely and effectively.

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MKS- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **SG-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **SMCB**- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation, study design, statistical analysis and interpretation; **SNG** - Review manuscript, literature survey and preparation of figures; coordination and manuscript revision.

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