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COMPARATIVE STUDY BETWEEN KETAMINE, PROPOFOL (1:3) VERSUS PROPOFOL ALONE IN SHORT SURGICAL PROCEDURES.

Anaesthesiology

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ABSTRACT

Introduction: TIVA has many advantages over inhalational anaesthesia. Ketamine and Propofol are mediations commonly used for TIVA as sole anaesthetic agent & have played safe and effective role. Opposing physiologic effect of ketamine & propofol suggest potential for synergy, this has led to interest in their combine use commonly termed as "KETOFOL". Because of potential advantages of KETOFOL over ketamine or propofol alone, it can be called "HOLY GRAIL". **Methods:** It is Hospital based randomized prospective study comprising of 2 groups with 40 patients in each Group A: combination of Ketamine(0.5mg/kg) + Propofol(1.5mg/kg) Group B: Propofol(1.5mg/kg) alone. Both groups received pre medication with Glycopyrrolate(0.004mg/kg), fentanyl(2mcg/kg) and midazolam(0.03mg/kg). Patients were observed for loss of eyelash reflex, incision time, total drug used, hemodynamic changes and adverse effects. Patients were monitored for 1 hour duration from time of induction to recovery room for hemodynamic changes and respiratory rate using Modified ALDRET's Scale. **Results:** On comparison Group A showed lower mean time of loss of consciousness, higher blood pressure & mean arterial pressure, higher ALDRET score & lower VAS score.Study showed that Ketofol has several benefits because of hemodynamic stability, lack of respiratory depression, early recovery & potent post procedural analgesia. Therefore, Ketofol should be an ideal agent for short surgical procedures.

KEYWORDS

Propofol, Fentanyl, Total Intravenous Anaesthesia, Short surgical procedure

INTRODUCTION

General anaesthesia has undergone a vast number of improvements and modifications and even its recently modified form Total intravenous anaesthesia (TIVA; induction and maintenance of anaesthesia with intravenous agents only) has undergone many improvements ever since its introduction into clinical practice. TIVA has many advantages over inhalational anaesthesia such as:

- No operating room pollution.
- Used in day care surgeries.
- No sophisticated delivery system required.
- Minimal cardiac depression.
- Decreased oxygen consumption.
- Avoids post operative hypoxia.
- Decreased incidence of PONV.
- It can also be used in remote settings apart from its use in well-equipped hospital.

Ketamine and Propofol are two medications commonly used for TIVA because they possess many of the desired characteristics including rapid induction and recovery respectively. However, Ketamine has lost favour with anesthesiologists due to propensity to cause emesis and recovery agitation, and its prolonged recovery time compared with that of Propofol[1].

Intravenous Propofol is currently a popular induction agent for surgical anaesthesia. It acts through potentiation of GABA-A receptor activity, thereby slowing the channel closing timeand also acting as a sodium channel blocker. Recent research has also suggested the endocannabinoid system may contribute significantly to Propofol's anaesthetic action and to its unique properties. These are prolongedapnoea[2], excitatory movements, significant decrease in mean arterial pressure, pain on injection[3]. Subsequently, there is an increase in the use of Propofol due to its favourable pharmacokinetics[4]. However, Propofol is associated with dose-dependent respiratory depression (especially when combined with opioids), hypotension and has no intrinsic analgesic property.

The opposing physiologic effects of Ketamine and Propofol suggest the potential for synergy, and this has led to interest in their combined use, commonly termed "Ketofol". The potential advantages of Ketofol over Propofol alone include the provision of deep sedation with lower doses of Propofol, thus potentially limiting Propofol-associated adverse respiratory effects; the provision of Ketamineanalgesia without the increased adverse respiratory effects associated with concomitant opioid administration; and the mitigation of Propofol-induced hypotension. The potential advantages of Ketofol over Ketamine -alone procedural sedation include shorter recovery time and a lower incidence of Ketamine associated emesis and recovery agitation(5-12)

One such agent under studies and also proved in various trials is KETOFOL i.e. combination of (Ketamine + Propofol) and may be called as " HOLY GRAIL", which has almost all the qualities as mentioned above and at the same time overcomes the adverse effects of individual drug.

MATERIALS AND METHODS

Study Area: The study was conducted at Government Medical College and Associated Hospitals, Kota from March 2021 to July 2022 after clinical approval of institutional ethical clearance committee.

Sample Size: 80 patients scheduled for short surgeries were taken on the basis of simple random sampling method.They were randomly divided into two groups of 40 patients each.

Inclusion Criteria

A. Patient of either sex, age between 20-60 yrs.
B. Patient belonging to ASA grade I&II.
C. Short surgical procedures of duration <30 minutes

Exclusion Criteria

A. Patients with co-morbid conditions like diabetes mellitus, asthma, hypertension etc.
B. Patient with known hypersensitivity to the drugs used in study
C. Patient who refuses to procedure

Pre-anaesthetic Assessment: Standard protocol were followed for pre anaesthetic assessment of patients.

Procedure:

Informed and written consent taken from each patient after complete explanation about the study protocol and the procedure.Visual Analogue Scale was shown to the patients and ability of patients to understand it was confirmed. Following preloading with ringer's

lactate 5-8 ml/kg Inj. Glycopyrrolate 0.004mg/kg, Fentanyl 2mcg/kg and Midazolam 0.03mg/kg were given.

Drug and Dosage:
Group A: 1:3 combination of Ketamine (0.5mg/kg) and Propofol (1.5mg/kg)

Group B: Propofol (1.5mg/kg) alone

Monitoring -Patients were monitored for HR, SBP and DBP during Induction: intra-op (at 0,1,2,3,4,5,10,15,20,25,30 minutes) and in post operative recovery room every 5 minutes for 1 hour (35,40,45,50,55,60 minutes). Patients were also monitored for post operative nausea and vomiting , delirium and emergence reaction. Duration of surgery, recovery characteristics (activity, respiration, circulation) were noted. All the complications and adverse reactions were managed according to standard treatment protocols of our institute.

Outcome Variables
Induction
1. Time to loss of eye lash reflex
2. Time for incision
3. Total drug used
4. Adverse Events
5. Hemodynamic changes;

Intra-op Characteristics
1. Hemodynamic changes
2. Supplementation of Opioids
3. Additional drugs
4. Adverse Event

Post-op Characteristics:
1. Hemodynamic changes
2. PONV
3. Respond to verbal command
4. Return of airway reflex
5. Recovery time
6. VAS Score

Recovery scale-Modified Aldrete Scale is a simple numeric scale for discharge of patient with points of 9 or10 measured at the end of anaesthesia and1hr into the post operative period.

Table 1 Modified Aldrete Scale:

Assessment items	Condition	Grade
Activity, able to move, voluntarily or on command	4 extremities	2
	2 extremities	1
	No	0
Breathing	Able to breathe deeply & cough freely	2
	Dyspnea, shallow or limited breathing	1
	Apnea	0
Consciousness	Fully awake	2
	Arousable on calling	1
	Unresponsive	0
Circulation (BP)	±20% of pre-anesthesia level	2
	±20% to 49% of pre-anesthesia level	1
	±50% of pre-anesthesia level	0
SPO_2	Maintains SpO_2 >92% in ambient air	2
	Maintain SpO_2 >90% with O_2	1
	Maintain SpO_2 <90% with O_2	0

Maximum score= 10. Low score = equal or less than 6. High recovery score= 7-10.

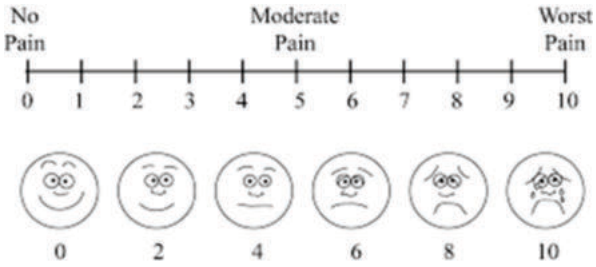

Figure 1-VAS : Visual Analouge Scale

RESULTS
Table No.2 - Time of Loss of Consciousness

Variables	Group A		Group B		P value
	Mean	SD	Mean	SD	
Time of loss of consciousness (in sec)	43.05	9.09	90.7	8.45	0.0001

Mean time to loss of consciousness was significantly lower in Ketofol group compared to Propofol group (43.05 vs 90.7 sec; $p < 0.05$).

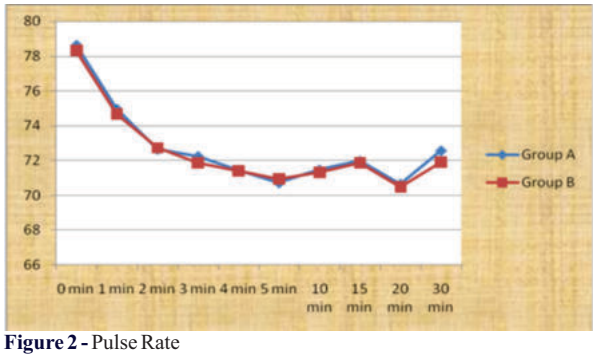

Figure 2 - Pulse Rate

No significant variation was observed in mean pulse rate between the two groups during the course of surgery ($p > 0.05$).

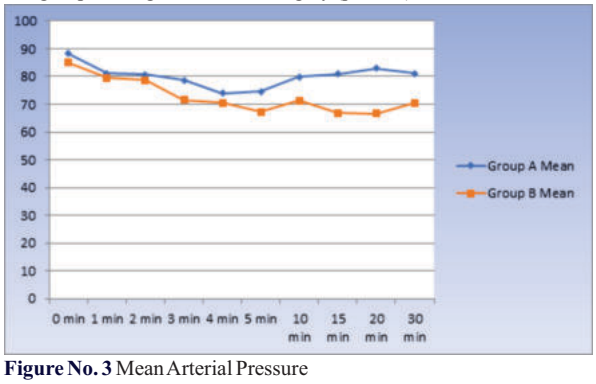

Figure No. 3 Mean Arterial Pressure

Significantly lower mean arterial pressure was observed in group b during major part of surgery (3,4,5,10,15,20,30 minutes)

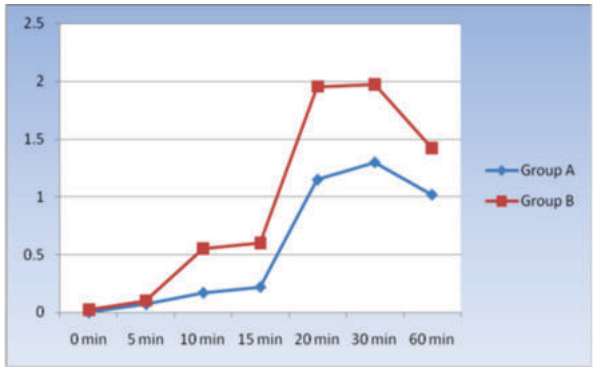

Figure No. 4 - Modified Alderts Score

Significantly higher Aldert's score was observed in the Ketofol group compared to Propofol group ($p < 0.05$)

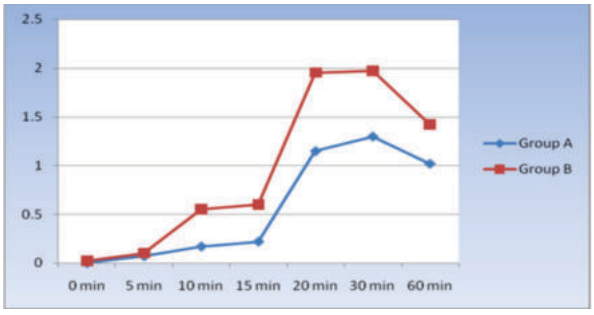

Figure No. 5 VAS Score:

Significantly lower VAS score was observed in the Ketofol group compared to Propofol group patients at,10, 15 and 60 minutes of surgery ($p < 0.05$).

DISCUSSION

Our study was conducted with the aim of comparing recovery characteristics, quality of anaesthesia and incidence of adverse events with Ketofol (1:3 combination of Ketamine 0.5 mg/kg and Propofol 1.5 mg/kg) versus Propofol 1.5 mg/kg alone for short surgical procedures.

In our study, results were consistent with Green S et al13 study, mean time to loss of consciousness was significantly lower in Ketofol group compared to Propofol group (43.05 vs 90.07 sec; $p < 0.05$).

No significant variation was observed in mean pulse rate between the two groups during the course of surgery ($p > 0.05$). Significantly lower mean systolic and diastolic blood pressure was observed in the Propofol group during the most part of surgery ($p < 0.05$).

Significantly higher Aldert's score was observed in the Ketofol group compared to Propofol group ($p < 0.05$). No significant difference was observed between groups on the basis of occurrence of post-operative cough and nausea/ vomiting ($P > 0.05$).Results were consistent with Akin A et al14 study.

In our study, results were consistent with Shah et al study, we observed a faster recovery in Ketofol group. Ketofol produced slightly faster recovery mean time of loss of consciousness was significantly lower in Ketofol group.

In our study we found No significant difference in incidence of post operative nausea/vomiting and cough in both groups, same results were observed by Shah et al.

In present study we found Ketofol to be both safe and efficacious but larger randomized, prospective studies are needed to further validate our findings.

CONCLUSION:

Ketofol is a combination of Ketamine and Propofol. It is an agent of choice for various procedures. The combination of Propofol and Ketamine has several benefits because of the hemodynamic stability, lack of respiratory depression, good recovery and potent post-procedural analgesia. Therefore, Ketofol should be an ideal combination drug for procedural sedation but larger randomized, prospective studies are needed to further validate our findings.

Conflict Of Interest:

There is no conflict of interest between author.

Abbreviations:

- TIVA - Total Intravenous Anaesthesia
- ASA -American Society of Anaesthesiologist
- MAP - Mean Arterial Pressure
- VAS - Visual Analog Scale

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