Section: Anaesthesia

Original Research Article

A COMPARISON BETWEEN 2 DIFFERENT PROPORTIONS OF KETAMINE-PROPOFOL AND PROPOFOL-FENTANYL FOR PROCEDURAL SEDATION AND ANALGESIA FOR MINOR GYNAECOLOGICAL PROCEDURES: A PROSPECTIVE RANDOMIZED CONTROL TRIAL

RM. Somanathan[1], J. Arul[2], K. Shahul Hameed[3]

[1-3]Assistant Professor, Government Stanley Medical College, Chennai, India.

Received : 18/12/2023
Received in revised form : 18/02/2024
Accepted : 02/03/2024

Keywords:
Airway Management Blood Pressure Propofol Ketamine Fentanyl, Postoperative pain.

Corresponding Author:
Dr. J. Arul
Email: drjarul@gmail.com

DOI: 10.47009/jamp.2024.6.2.156

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (2); 756-760

Abstract

Background: Procedural Sedation and Analgesia (PSA) involves a reduction in patient's degree of awareness while maintaining airway control and haemodynamics at the same time. This study aims to compare Ketamine-Propofol and Propofol-Fentanyl for Procedural Sedation in minor gynaecological procedures. **Aim and objectives:** To study the duration and level of sedation, hemodynamic and respiratory profiles, quality of analgesia of Ketamine-Propofol and Propofol-Fentanyl for Procedural Sedation in minor gynaecological procedures. **Material & Methods: T**hree groups of thirty patients were selected and allotted into three groups. Group 1- Received ketamine-propofol intravenously (IV) in ratio of 1:1. Group 2 - Received ketamine-propofol in ratio of 1:2. Group 3 - Received fentanyl-propofol mixture. All the three study drugs were given till a Ramsay Sedation Score of 5-6 was achieved. **Results:** Three groups were demographically similar. Duration of surgery was similar. Heart rate, respiratory rate, systolic and diastolic blood pressure were similar between the groups. Ramsay sedation score, EVANS/PRST Score and Wong Bakers pain score were significant at 15 min, at end of procedure and 15 min after procedure. **Conclusion:** We conclude that propofol: fentanyl group had better postoperative pain relief and faster recovery time.

INTRODUCTION

Procedural sedation is described by American college of emergency physicians as "a technique of administering dissociative agents or sedatives with or without analgesics to induce a state that allows patients to tolerate unpleasant procedures while maintaining stable cardiorespiratory function".

PSA involves a reduction in patient's degree of awareness while maintaining airway control and stable haemodynamics at the same time.

PSA needs proper planning and should be provided under careful monitoring with proper preanaesthetic workup and emergency measures readily available.

Three such drugs found most suitable for this technique are ketamine, propofol and fentanyl. This study aims to compare the characteristics of these drugs when used in combination and their usefulness in minor gynaecological procedures.

Aims and Objectives of the Study

Aim

The present study is initiated to compare two different solutions consisting of ketamine and propofol in concentrations of 1:1 and 1:2 with reference to duration and level of sedation, hemodynamic and respiratory profiles, quality of analgesia and to compare the above effects with propofol-fentanyl combination for minor gynaecological procedures.

Objectives

Primary Objectives

- Assessing the time taken for required sedation/level of sedation (RSS 5-6), the depth of anaesthesia / awareness under anaesthesia and the recovery time.
- Hemodynamics and any complications also monitored.

MATERIALS AND METHODS

A prospective, double blinded, randomized study was conducted in patients undergoing minor elective gynaecological procedures. After getting approval from the Institutional Ethics Committee and obtaining written informed consent from all participants (on the day before surgery), 90 adult

ISSN (O): 2687-5365; ISSN (P): 2753-6556

female patients between 18 and 50 years of age with ASA physical status 1 and 2 assessment and with mallampatti airway classes 1 and 2 were enrolled for the study based on the inclusion and exclusion criteria.

Inclusion Criteria

- Consenting adult females aged 18-50 years
- Weight 40-70kg
- ASA 1 and ASA 2 PS classes of patients
- Patients undergoing elective non laparoscopic minor gynaecological procedures.

Exclusion Criteria

- Patient refusal
- Mallampatti airway classes 3 and 4
- Patient weight > 70 kg and <40 kg
- Emergency surgery or laparoscopic surgeries
- History of drug abuse/psychiatric illness/head injury
- Known Hypersensitivity to propofol or ketamine / allergy to eggs

Materials

Drugs - intravenous ketamine, propofol, fentanyl, glycopyrrolate, midazolam, oral ranitidine, inj ondansetron, inj adrenaline, inj atropine, inj succinylcholine and other emergency drugs as required.

Primary Objectives

- Assessing the time taken for required sedation/level of sedation maintained intraoperatively.
- Assessing the depth of anaesthesia / awareness under anaesthesia.
- Monitoring hemodynamic and respiratory parameters.
- Assessing the recovery time.

Secondary Objectives

- Post-operative pain relief.
- Assessing amount of drug consumed.
- Adverse effects.

The patients were randomized into 3 study groups (1/2/3) by 'Sequentially Numbered Opaque Sealed Envelopes'(SNOSE) schemes with 30 patients each. A sample size of 30 patients in each group was calculated so as to have a power of 80% and an alpha error of 0.05 to detect the expected differences among the three groups with respect to the mean Ramsay sedation score (RSS) with a confidence interval of 95%.

Study groups

Study population was divided into 3 groups of 30 patients each.

Group 1- Received ketamine-propofol intravenously (IV) in ratio of 1:1. Prepared by adding 2ml of 50mg/ml ketamine to 10ml of 10mg/ml propofol in a single 20 cc syringe. Given in 3ml aliquots as initial dose until an adequate sedation of RSS 5-6 (Ramsay sedation scale) was achieved.

Group 2 - Received ketamine-propofol in ratio of 1:2. Prepared by adding 1ml of 50mg/ml ketamine and 1 ml of distilled water to 10mg/ml propofol in a single 20 cc syringe. 3ml IV given as initial dose repeated until a RSS of 5-6 was achieved.

Group 3 - Received fentanyl-propofol mixture. Prepared in a single 20 cc syringe with 2ml of 50mcg/ml fentanyl and 10ml of 10mg/ml propofol and given in 3ml aliquots IV as initial dose and repeated until a RSS of 5-6 was achieved.

Monitoring

All the patients were premedicated with oral ranitidine 150 mg (2 hrs prior to procedure) and with injections midazolam 0.03 mg/kg IV, and glycopyrrolate 0.2 mg IV 15 minutes before induction. The study group was double blinded with three different anaesthesiologists involved. The drug was prepared by an anaesthesiologist not involved in the study. All drug combinations were prepared in a single 20 cc syringe. All drug preparations were of the same colour and quantity and so there was no way of identifying the drug mixture given to the anaesthesiologist involved with the case. ECG, Pulse oximeter, NIBP, EtCO2, connected. Initial dose 3ml given in all 3 groups and repeated till RSS score of 5-6 was reached. Then patient was put in operating supine/lithotomy position for surgery and the operating surgeon was asked to proceed. The level of sedation will be monitored intraoperatively, i.e. RSS was monitored 5 minutes after induction,15 minutes after induction, at the end of procedure and 15 minutes postoperatively.

- The depth of anaesthesia/awareness under anaesthesia was monitored using the PRST scoring (EVANS Score). A score of <3 was considered to be adequate depth of anaesthesia.
- The recovery time was defined as the time taken from the administration of last dose of the study drug to the point when patient achieved a Modified Aldrete score of 9-10.
- The postoperative rating for pain was done using Wong-Baker FACES pain scale 0/5/10/15 minutes after the procedure. If pain rating >4, then post-op rescue analgesia Inj.Tramadol 25mg IV was given as a onetime dose.
- The duration of the surgery (time taken from skin incision until the last skin stitch) was be noted.
- The total drug consumed in each patient was noted. (The number of intra operative boluses required to maintain sedation will also be noted)
- The adverse effects such as apnea, bradycardia, hypotension, rash, seizure, myoclonus and airway intervention during the procedure and emergence phenomena such as agitation, hallucinations and vomiting after the procedure were recorded.
- Inj. Ondansetron 4mg iv was given in case of postoperative nausea and vomiting.

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RESULTS

The collected data were entered in Excel 10 and analysed with IBM SPSS (Statistical package for social services) statistics software 23.0 Version. Describing the data descriptive statistics frequency analysis was done by percentage analysis for categorical variables and mean & S.D(Standard deviation) for continuous variables. The one-way ANOVA test was used to find the significant difference in the multivariate analysis. Chi-Square test was used to find the significance in categorical data. The probability value .05 - considered as significant level in all the above statistical tools Both the groups were similar with respected demography.

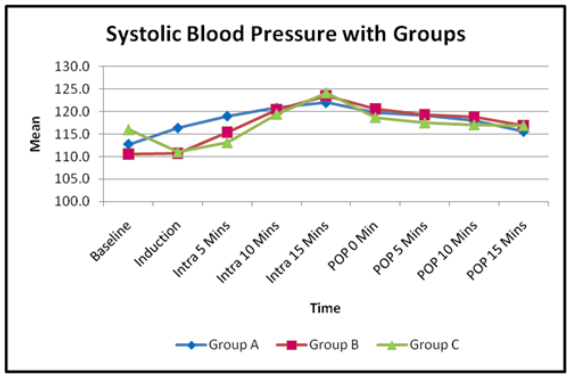

Figure 1

The above table shows comparison of Systolic Blood Pressure with Groups by One-way ANOVA were all the time durations of Systolic Blood Pressure shows no statistical significant difference at p>0.05 level except Systolic Blood Pressure at Induction (F-value=3.326, p=0.041<0.05) which shows statistical significant difference at p<0.05 level.

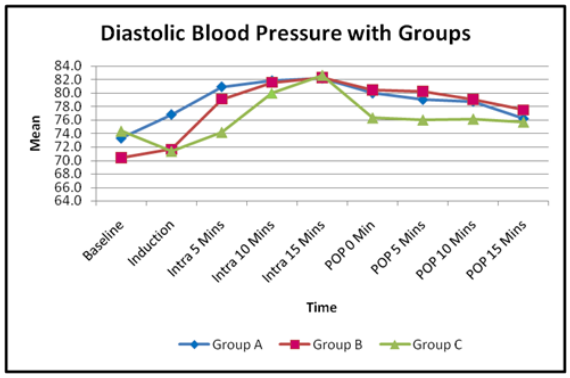

Figure 2

The above table shows comparison of Diastolic Blood Pressure with Groups by One-way ANOVA were all the time durations of Diastolic Blood Pressure shows no statistical significant difference at p>0.05 level except Diastolic Blood Pressure at Intra 5 mins (F-value=3.652, p=0.030<0.05) which shows statistical significant difference at p<0.05 level. Comparison of SpO2, Respiratory rate, ETCO2, Heart rate were not significant between the groups. comparison of Ramsay Sedation Score with Groups by One-way ANOVA were all the time durations of Ramsay Sedation Score shows no statistical significant difference at p>0.05 level whereas in comparison of Ramsay Sedation Score at 15 mins (F-value=11.22, p=0.0005<0.01), Ramsay Sedation Score at End of Procedure (F-value=14.03, p=0.0005<0.01) and Ramsay Sedation Score at POP 15 mins (F-value=28.894, p=0.0005<0.01) which shows statistical significant difference at p<0.01 level.

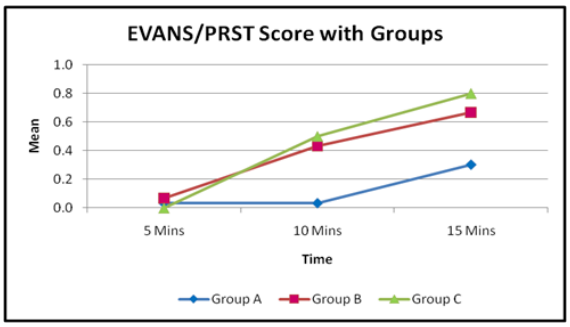

Figure 3

The above table shows comparison of EVANS/PRST Score with Groups by One-way ANOVA were in comparison of EVANS/PRST Score at 5 mins (F-value=1.024, p=0.364>0.05) which shows no statistical significant difference at p>0.05 level whereas in comparison of EVANS/PRST Score at 10 mins (F-value=5.974, p=0.004<0.01) which shows statistical significant difference at p<0.01 level. Similarly in comparison of EVANS/PRST Score at 15 mins (F-value=3.38, p=0.039<0.05) which shows statistical significant difference at p<0.05 level.

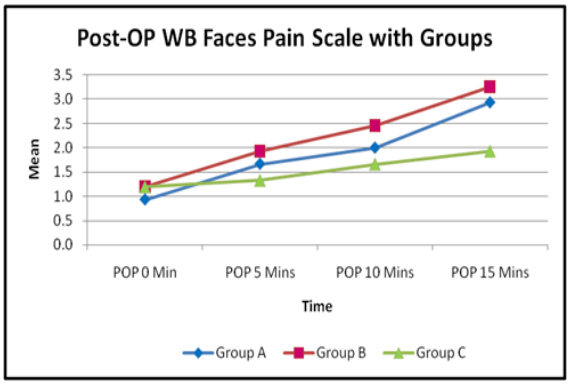

Figure 4

The above table shows comparison of Post-OP WB Faces Pain Scale with Groups by One-way ANOVA were all the time durations of EtCO2 shows no statistical significant difference at p>0.05 level whereas Post-OP WB Faces Pain Scale at POP 10 mins (F-value=4.127, p=0.019<0.05) which shows statistical significant difference at p<0.05 level.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Similarly, in comparison of Post-OP WB Faces Pain Scale at POP 15 mins (F-value=8.875, p=0.0005<0.01) which shows statistical significant difference at p<0.01 level.

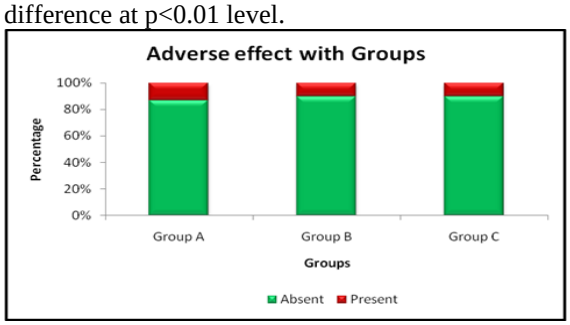

Figure 5

The above table shows comparison between Adverse effect with Groups by Pearson's chi-squared test were $\chi 2=0.225$, p=0.894>0.05 which shows no statistical significant association between Adverse effect and Groups. p=0.023<0.05Surgery duration/ shows no statistical significant difference between Groups. Comparison of Total drug consumed and recovery time with Groups shows highly statistical significant difference (p=<0.01).

Table 1: Comparison of Ramsay Sedation Score with Groups by One-way ANOVA

Variable	Groups	N	Mean	S.D	F-value	p-value
Induction	Group A	30	5.5	0.5	1.115	0.332 #
	Group B	30	5.7	0.5		
	Group C	30	5.5	0.5		
5 Mins	Group A	30	5.5	0.5	1.197	0.307 #
	Group B	30	5.6	0.5		
	Group C	30	5.4	0.5		
15 Mins	Group A	30	4.5	0.5	11.22	0.0005 **
	Group B	30	4.4	0.6		
	Group C	30	3.9	0.5		
End of procedure	Group A	30	4.2	0.5	14.03	0.0005 **
	Group B	30	4.1	0.5		
	Group C	30	3.5	0.7		
POP 15 Mins	Group A	30	3.3	0.7	28.894	0.0005 **
	Group B	30	3.2	0.5		
	Group C	30	2.3	0.5		
# No Statistical Significance at p > 0.05,** Highly Significant at p < 0.01						

Table 2: Comparison between Adverse effect with Groups

			Groups			Total	χ 2 - value	p-value
			Group A	Group B	Group C			
Adverse effect	Absent	Count	**26**	**27**	**27**	**80**	0.225	0.894 #
		%	86.7%	90.0%	90.0%	88.9%		
	Present	Count	4	3	3	10		
		%	13.3%	10.0%	10.0%	11.1%		
Total		Count	30	30	30	90		
		%	100.0%	100.0%	100.0%	100.0%		
# No Statistical Significance at p > 0.05 level								

DISCUSSION

Total intravenous anaesthesia(TIVA) has been the norm for day care surgeries in recent times. Many drugs have been used in TIVA but the commonly used ones include ketamine, propofol and fentanyl. The data in this study proves that both ketamine and propofol can be used in different proportions for sedoanalgesia to good effect.

Time taken to predetermined sedation level and depth of sedation

Our study used Ramsay sedation score to assess sedation goal and EVANS scoring to assess depth of anaesthesia. Sadeq et al1, concluded that ketofol in proportions of 1:1 and 1:2 had similar sedation onset times, an observation which is not consistent with our study which observes a faster induction time with the ketamine-propofol 1:1 group. Bahrami et al2 observed that both propofol-ketamine and propofol-fentanyl groups had similar sedation onset and depth. Senthil et al3found that depth of anesthesia was better maintained with ketamine 1.5 mg/kg than with ketamine 0.5 mg/kg and 1 mg/kg. Also they noted that more supplementary doses of drugs were required to maintain anaesthesia in the groups containing lower doses of ketamine, which is consistent with our study.

Hemodynamics

Slavik et al4 compared 8 clinical trials (which used propofol and ketamine) in their study and found statistically significant lower mean arterial pressures in the groups receiving propofol alone. With regards to respiratory rate, heart rate and oxygen saturation, they found no statistical significance. Our study shows that hemodynamics, with the exception of SpO2 and EtCO2, are comparable in all 3 groups. Lower oxygen saturation levels and slightly higher EtCO2 recordings (in immediate post-operative period) are noted in the propofol-fentanyl group.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Recovery times and post-operative pain relief

Daabiss et al,[5] and Singh et al,[6] concluded in their studies that the propofol-fentanyl(PF) study population was associated with better pain relief in the immediate postoperative period. They also reported shorter recovery and mean discharge times in the PF group. This finding is consistent with our study as well.

Adverse effects

With regards to effects, our study reports no statistical difference between adverse incidences among the 3 groups. Nausea, vomiting and hypotension are the common side effects noted. Apnea occurred in 2 patients, 1 each in groups 2 and 3, which shows no statistical significance. Khajavi et al,[7] reported similar results with their study. **Tosun et al,[8] reported higher incidence of apnea and hemodynamic instabilty intraoperatively in the fentanyl-propofol group. Total drug usage**

In our study, considerably higher drug requirements are noted in groups 2 and 3, when compared with group 1. Kurdi et al,[9] observed that higher propofol requirement was noted in the propofol-fentanyl group, which is similar to our observation. They also noted that depth of anaesthesia was better in the ketofol 1:2 group and post-operative pain relief was better in the ketofol 1:1 group.

Among other studies, Ayatolahi et al,[10] reported effective sedoanalgesia with ketofol (2:1) in children undergoing bone marrow aspiration. Better patient satisfaction and lack of any significant complications was observed in the study.

Arora.S,[11] reviewed 6 clinical trials in his study and reported that though ketofol appeared to be a safe and efficacious agent of use for PSA, the literature was not strong enough to definitively conclude that ketofol was better than either agent alone or than either agent used in combination with a different agent.

Yalcin et al,[12] compared efficacy of ketamine alone, propofol alone and ketamine-propofol combination in chidren undergoing dental treatment. They observed that ketamine plus propofol treatment was linked with lower complication and higher satisfaction rates than with either drug used alone.

Limitations of our study

There are not many studies with regards to the changes in the physicochemical characteristics/stability of a single syringe combination of ketofol or propofol-fentanyl. The difference in characteristics like age and body weight may be confounding factors in our study, the reason being people with higher age and lower body weights may require lower drug dosages than fellow participants. This may affect outcome. The use of an opioid, fentanyl in one of the study groups may affect outcome with regards to pain relief.

CONCLUSION

We conclude in our study that ketamine: propofol in the ratio of 1:1 is better in terms of faster induction, lower drug consumption but with the prolongation of recovery time and lesser post-operative pain relief. There is no significant difference in terms of hemodynamics, depth of anaesthesia maintained intraoperatively and incidence of adverse effects between the three groups. Better postoperative pain relief and faster recovery time is noted with the propofol: fentanyl group.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556