Section: Anaesthesiology

Original Research Article

COMPARATIVE STUDY OF TWO DRUGS COMBINATION IN TOTAL INTRAVENOUS ANAESTHESIA: PROPOFOL - KETAMINE VS PROPOFOL - FENTANYL

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ABSTRACT

Background: Total intravenous anesthesia (TIVA) is a technique of general anesthesia using the agents solely by IV route in the absence of all inhalations and nitrous oxide, but an ideal anesthetic combination has to be selected to maintain the hemodynamic status and to avoid undesirable side effects. **Materials and Methods:** Out of 120 patients, 60 (group I) were administered propofol 1 mg/kg body weight and ketamine 1 mg/kg body weight given as a bolus dosage, and 60 (group II) were given propofol 1 mg/kg body weight and fentanyl 2 mcg/kg body weight as a bolus dose pre-induction, induction, intraoperative, and postoperative anesthetic stages. Systolic BP and diastolic BP at different stages were compared and recorded. Moreover, postoperative side effects were also noted. **Result:** There was a significant p-value in induction and intraoperative stages of anesthetics and hemodynamic profile ($p<0.001$), but postoperative stages of anesthesia and systolic and diastolic BP were almost equal in both groups ($p>0.001$); hence, the p-value was insignificant with negligible postoperative side effects. **Conclusion:** It is proved that even though there are differences regarding hemodynamic stability and recovery, both propofol-ketamine and propofol-fentanyl combinations are ideal alternatives to gaseous anesthetic agents in elective surgeries.

INTRODUCTION

Total intravenous anesthesia (TIVA) is a technique of general anesthesia using a combination of agents given solely by the intravenous route in the absence of all inhalation agents and nitrous oxide. The induction of intravenous anesthetic should be sufficient to ensure that the patient loses consciousness but not to cause undesirable side effects such as arterial hypotension and bradycardia/tachycardia.[1] TIVA has an important role in day care procedures requiring a short duration of anesthesia with smooth emergence from anesthesia. It is reported that comparing the combination of propofol-fentanyl and propofol-ketamine proved propofol-ketamine to be safe and satisfactory with less intraoperative hemodynamic disturbances and postoperative psychotic disturbances for TIVA.[2] It is also noted in recent studies that propofol-fentanyl has better recovery characteristics, like awakening time and response to verbal commands, compared to the propofol-ketamine combination.[3] Still controversy exists about the ideal combination of these anesthetic agents for TIVA.[4] Hence, an attempt is made to compare and evaluate the pros and cons of hemodynamic stability and other severe side effects in intraoperative and postoperative periods..

MATERIALS AND METHODS

120 (one hundred twenty) patients posted for short surgical procedures (duration <2 hours) under general anesthesia of GSL Medical College Hospital, Rajahmundry, Andhra Pradesh-533296, were studied.

The duration of the study was one year i.e from October 2024 to November 2025

Inclusive Criteria: Patients of ASA-I and ASA-II groups aged between 20 to 60 years, ready for elective surgery gave their consent in writing for study were selected.

Exclusion Criteria: Patients having a history of allergy to particular drugs or allergy to fat or egg,

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Pregnant females, patients on monoamine oxidase inhibitors, history of jaundice, age above 50 years of age, not ready to undergo elective surgery lasting more than 80 minutes. Immunocompromised patients were excluded from the study.

Method: As premedication tablets, Ranitidine 150 mg + Alprazolam 0.25 mg were given the night before and 2 hours before the induction of surgery.

Anaesthesia technique: standard anesthetic technique was used in every patient. After securing the intravenous line, monitoring gadgets were attached, which included ECG, SPO2, and a non-invasive BP cuff. Baseline parameters were observed and recorded. Injection of midazolam 1mg I.V. was given 2 minutes before the induction of anesthesia in both groups.

Induction of anesthesia of patient Group I was administered with propofol 1.0 mg/kg body weight and ketamine 1.0 mg/kg body weight given as a bolus dosage. Group II was administered with propofol 1mg/kg body weight and fentanyl 2 mcg/kg body weight given as IV bolus doses.

In both groups, injection of succinylcholine was given as a muscle relaxant before intubation in doses of 1.5 mg/kg body weight with maximum doses not exceeding 100 mg. Patients were ventilated with 100% oxygen via face mask for 60-90 seconds and intubation was done with an appropriately sized cuffed endotracheal tube. Hemodynamic and other monitoring parameters were observed continuously and recorded at an interval of 1 minute each for the first 5 minutes.

Maintenance of anesthesia: In group I, maintenance of anesthesia was achieved with infusion of propofol 2mg/kg/hr and ketamine 2 mg/kg/h, while in group II, maintenance of anesthesia was achieved with infusion of propofol 2mg/kg/h and fentanyl 2 mcg/kg/h. vecuronium Bromide was used as a muscle relaxant in the dosage of 0.1 mg/kg body weight as an initial bolus dose and supplemented with top-ups of 1 mg in both groups. Hemodynamic and other monitoring parameters were observed continuously and noted at intervals of 5 minutes during the operation. Patients were ventilated with 100% oxygen with a closed circuit attached to a circle absorber system.

Reversal of relaxant effect: All the anesthesia drugs were stopped 10 minutes before the anticipated end of surgery. At the end of surgery, neuromuscular blockade was reversed with an injection of neostigmine 40 µg/kg body weight and an injection of glycopyrrolate 10 µg/kg body weight, which was given over 2-3 minutes. Extubation was done when the patient was able to maintain rhythmic respiration and adequate tidal volume. BP and SPO2 were monitored regularly.

Statistical Analysis: Various parameters such as mean pulse rate, systolic and diastolic BP recovery (wakefulness), and postoperative side effects were compared with the t-test and recorded. The statistical analysis was carried out using SPSS software. The ratio of male female was 2:1.

RESULTS

Table-1: Comparison of mean pulse rate of both groups at different stages of anaesthesia

- **Pre Induction:** both groups are compared at $p>0.95$ (p value is Insignificant)
- **Induction:** at 1 Minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes were compared in both groups and p value is highly significant ($p<0.001$).
- **Intra-Operative:** Comparison between both groups at different interval between 10 minutes to 60 minutes has significant p value ($p<0.001$)
- **Post-Operative group:** Comparison at different interval 1 minute, 5 minutes and 20 minutes interval has significant p value ($p<0.001$) but at 10 minutes and 15 minutes interval comparison was same hence p value was insignificant ($p>0.72$).

Table-2: Comparison of systolic blood pressure in both groups

- **Pre-Induction:** has insignificant p value ($p>0.81$), but at the interval 1 minute to 5 minutes of induction has significant p value ($p<0.001$).
- **In Intra-operative:** different interval of 10 minutes to 50 minutes has significant p value ($p<0.001$).
- **In post-**operative: Studies of different interval of 1 minute to 20 minutes had significant p value ($p<0.001$).

Table-3: Comparison of Diastolic blood pressure in both groups

- **Pre-Induction:** study was insignificant $p>0.74$, but at different interval of 1 minute to 5 minutes has significant p value ($p<0.001$).
- **Intra-Operative:** comparison studies at the interval of 10 minutes was insignificant but, at 20 minutes to 60 minutes interval has significant p value ($p<0.001$)
- **Post-Operative:** Comparison also had significant p value ($p<0.001$) except at 15 minutes.

Table-4: Comparison of wakefulness score of both group at different interval of 1 minute to 20 minutes has significant p value ($p<0.001$).

Table-5: In the comparison of post-operative side effects

- Nausea 1 (1.66%) in group-I, 3 (5%) in group-II
- Secretions 5 (8.3%) in group-I
- Post-ketamine sequelae 2 (3.3%)

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Table 1: Comparison of Mean pulse rate of both groups at different stages of anaesthesia in group-I and II

Total No. of patients 60+60=120

Anaesthesia stage	Time Interval	Group (60+60)	Mean SD	t test	p value
Pre-Induction	--	I II	84.05 (±5.15) 84.10 (±5.2)	0.05 (NS)	p>0.95
Induction	1 Min	I II	84.20 (±5.15) 76.30 (±4.52)	7.3	P<0.001
	2 Min	I II	90.5 (±5.20) 76.30 (±4.40)	8.94	P<0.001
	3 Min	I II	90.80 (±5.10) 77.32 (±4.30)	15.6	P<0.001
	4 Min	I II	90.72 (±2.15) 77.10 (±1.8)	15.8	P<0.001
	5 Min	I II	86.20 (±5.02) 85.16 (±4.32)	2.61	P<0.001
Intra-Operative	10 Min	I II	86.28 (±2.10) 85.20 (±4.33)	2.89	P<0.001
	20 Min	I II	84.60 (±2.20) 88.05 (±4.75)	5.06	P<0.002
	30 Min	I II	84.32 (±5.02) 87.65 (±4.62)	3.78	P<0.001
	40 Min	I II	84.92 (±5.15) 87.88 (±4.58)	3.32	P<0.003
	50 Min	I II	84.52 (±5.05) 87.06 (±4.45)	2.92	P<0.002
	60 Min	I II	84.25 (±4.04) 67.30 (±3.12)	2.57	P<0.003
Post-Operative	1 Min	I II	84.52 (±3.92) 89.20 (±2.98)	7.36	P<0.005
	5 Min	I II	84.32 (±4.12) 85.38 (±3.08)	2.19	P<0.001
	10 Min	I II	84.25 (±2.28) 84.28 (±3.88)	0.50 (NS)	P>0.61 (NS)
	15 Min	I II	84.88 (±5.35) 84.03 (±4.84)	0.91 (NS)	p>0.72 (NS)
	20 Min	I II	84.55 (±5.42) 89.15 (±5.02)	7.25	P<0.001

Table 2: Comparison of systolic Blood pressure in both groups at different stages of anaesthesia

Anaesthesia stage	Time Interval	Group	Mean SD	t test	p value
Pre-Induction	--	I II	125.92 (±9.50) 126.30 (±9.66)	0.21 (NS)	p>0.83 (NS)
Induction	1 Min	I II	125.28 (±5.22) 116.32 (±4.40)	10.1	P<0.001
	2 Min	I II	136.05 (±5.60) 122.12 (±4.32)	15.2	P<0.001
	3 Min	I II	135.65 (±3.64) 121.28 (±4.20)	15.7	P<0.001
	4 Min	I II	132.03 (±6.68) 121.08 (±3.42)	9.86	P<0.001
	5 Min	I II	130.36 (±5.25) 120.28 (±4.20)	11.5	P<0.001
Intra-Operative	10 Min	I II	129.25 (±4.20) 126.28 (±3.88)	4.02	P<0.002
	20 Min	I II	128.62 (±2.72) 130.24 (±3.14)	3.12	P<0.002
	30 Min	I II	128.28 (±3.22) 132.05 (±4.58)	5.21	P<0.001
	40 Min	I II	128.06 (±2.88) 130.28 (±3.42)	3.78	P<0.001
	50 Min	I II	127.88 (±4.32) 132.02 (±5.58)	4.54	P<0.001
Post-Operative	1 Min	I II	132.24 (±3.62) 136.12 (±5.52)	4.56	P<0.05
	5 Min	I II	128.38 (±3.75) 128.38 (±4.28)	0.024 (NS)	p>0.98 (NS)
	10 Min	I II	128.38 (±4.28) 126.22 (±2.12)	3.8	P<0.001
	15 Min	I II	128.04 (±3.28) 125.26 (±2.22)	5.43	P<0.001
	20 Min	I II	127.72 (±3.58) 123.64 (±2.34)	7.38	P<0.001

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Table 3: Comparison of Diastolic Blood pressure of both groups at different stages of anaesthesia

Anaesthesia stage	Time Interval	Group	Mean (±SD)	t test	p value
Pre-Induction	--	I II	80.53 (±3.52) 80.05 (±3.54)	0.74 (NS)	p>0.57 (NS)
Induction	1 Min	I II	80.88 (±3.52) 73.68 (±2.62)	12.7	P<0.001
	2 Min	I II	86.24 (±3.74) 75.30 (±2.52)	18.7	P<0.001
	3 Min	I II	86.62 (±3.82) 75.48 (±2.42)	19.08	P<0.001
	4 Min	I II	86.43 (±3.72) 75.38 (±2.53)	19.0	P<0.001
	5 Min	I II	86.92 (±3.53) 75.28 (±2.52)	19.65	P<0.001
Intra-Operative	10 Min	I II	81.83 (±2.62) 81.12 (±2.52)	1.2 (NS)	p>0.21 (NS)
	20 Min	I II	81.32 (±3.90) 83.43 (±2.52)	2.69	P<0.005
	30 Min	I II	81.36 (±2.98) 84.43 (±3.52)	5.15	P<0.001
	40 Min	I II	81.43 (±2.03) 83.92 (±3.35)	4.96	P<0.003
	50 Min	I II	81.32 (±4.32) 84.84 (±3.35)	4.98	P<0.002
	60 Min	I II	81.52 (±2.80) 85.23 (±3.32)	6.61	P<0.001
Post-Operative	1 Min	I II	82.03 (±4.04) 86.32 (±5.25)	5.01	P<0.001
	5 Min	I II	79.12 (±2.84) 80.86 (±3.16)	3.12	P<0.001
	15 Min	I II	78.68 (±2.32) 79.28 (±3.04)	0.91 (NS)	p>0.05
	20 Min	I II	78.52 (±1.12) 79.72 (±3.52)	3.93	P<0.001

Table 4: Comparison of recovery (wakefulness) score of both groups

Time Interval	Group	Mean (±SD)	t test	p value
1 Minutes	I II	--	--	--
5 Minutes	I II	0.42 (± 0.04) 0.66 (±0.03)	37.1	P<0.001
10 Minutes	I II	0.82 (±0.02) 1.05 (±0.03)	49.4	P<0.001
15 Minutes	I II	1.62 (±0.02) 1.73 (±0.04)	19	P<0.001
20 Minutes	I II	1.98 (±0.02) 2.03 (±0.04	8.6	P<0.001

Table 5: Comparison of post-operative side effects

Side effects	Group-I No	Percentage (%)	Group-II No	Percentage (%)
Nausea	1 (1.6%)	-	3 (5%)	-
Vomiting	-	-	-	-
Secretions	5 (8.3%)	-	-	-
Laryngoscope/ Bronchospasm	-	-	-	-
Post-ketamine squeal	2 (3.3%)	-	-	-
	-	-	-	-
	-	-	-	-
	-	-	-	-

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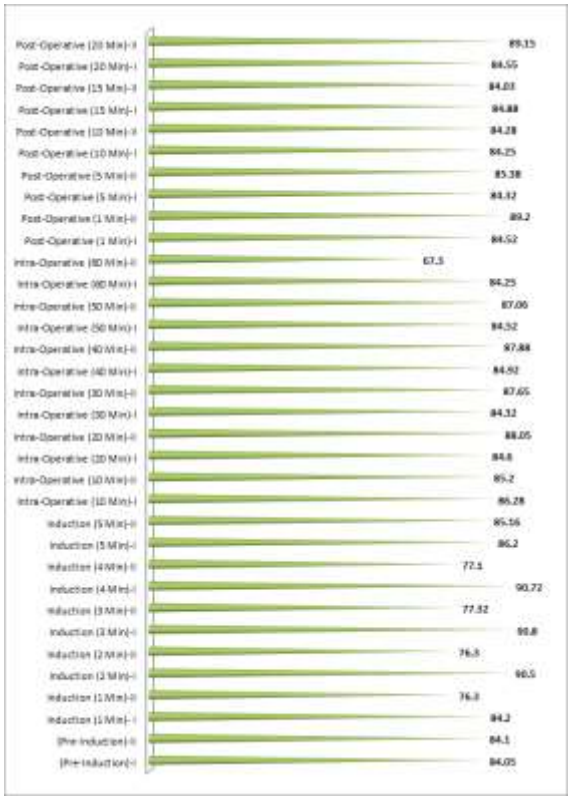

Figure 1: Comparison of Mean pulse rate of both groups at different stages of anaesthesia in group-I and II

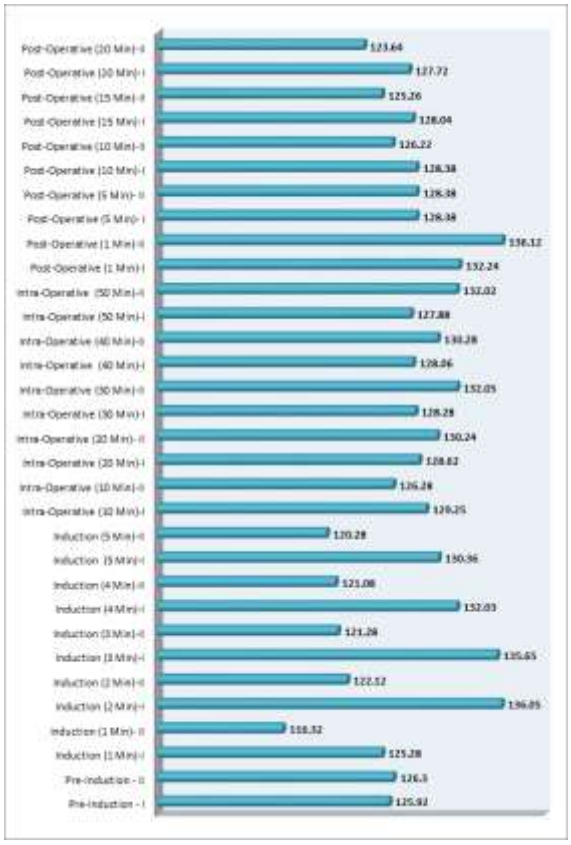

Figure 2: Comparison of systolic Blood pressure in both groups at different stages of anaesthesia

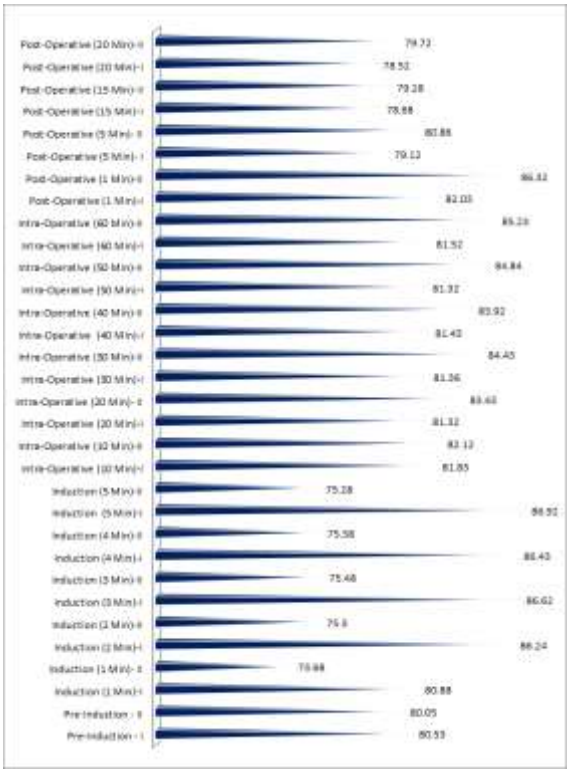

Figure 3: Comparison of Diastolic Blood pressure of both groups at different stages of anaesthesia

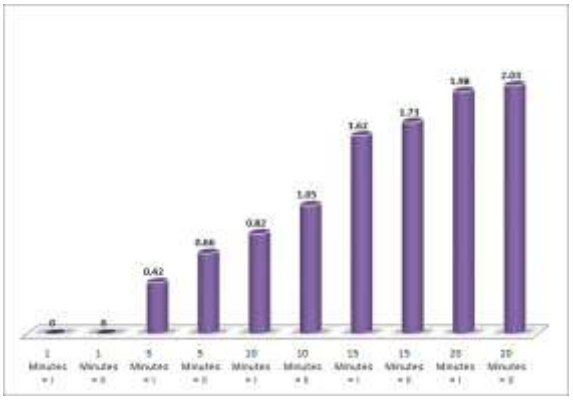

Figure 4: Comparison of recovery (wakefulness) score of both groups

DISCUSSION

Present a comparative study of two drug combinations, TIVA propofol and ketamine and propofol and fentanyl. In comparison of the mean pulse rate of both groups at different stages of anesthesia, the induction stage of 1 minute, 2 minutes, 3 minutes, 4 minutes, and 5 minutes have a similar p-value of <0.001. Intraoperative 10 minutes, 20 minutes, 40 minutes, 50 minutes, and 60 minutes and postoperative 1 minute and 5 minutes have significant p-values (p<0.001), but postoperative 10 minutes, 15 minutes, and 20 minutes had p>0.70 (p value was insignificant), i.e., the parameters of both parameters remain the same (Table 1). In systolic BP and diastolic BP postoperative time intervals of 5 minutes, 10 minutes, 15 minutes, and 20 minutes were almost equal; hence, the p-value was

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insignificant (p>0.24) (Tables 2 and 3). In the comparison of recovery (wakefulness) scores, 5 minutes and 10 minutes had a highly significant p-value (p<0.001), but at intervals of 15 minutes and 20 minutes, the parameters of both parameters are more or less in agreement with each other (Table-4). In the comparison of postoperative side effects, nausea was observed in 1 in group I and 3 in group II, and secretion was observed in 4 in group I (Table 5). These findings are more or less in agreement with previous studies.[5,6,7]

Anesthesia is seldom accomplished by a single drug because no single drug is able to provide all components of anesthesia without seriously compromising hemodynamic and/or respiratory function, reducing operating conditions, or postponing postoperative recovery. Because of the small therapeutic window, a detailed characterization of the concentration-effect relationships of anesthetics is required to allow a proper selection of the various TIVA drugs and the combinations thereof to obtain optimal therapeutic effect in the absence of significant side effects. During the past decades for propofol and the opioids fentanyl, ketamine, alfentanil, and sufentanil, considerable progress has been made in the characterization of the pharmacokinetics and pharmacodynamics of those drugs and of the combinations thereof.

The availability of rapid- and short-acting sedative hypnotics, analgesics, and muscle relaxants has refocused the attention on complete anesthesia by intravenous route. The advent of continuous infusion systems has made TIVA more popular and convenient. Propofol is a substitute for phenol anesthesia, which is associated with rapid smooth induction, good maintenance, and rapid recovery.[8] Ketamine is a potent analgesic that has a high margin of safety. It produces no negative influence on ventilation or circulation. Its main disadvantage is emergence delirium. Fentanyl, a phenyl piperidine derivative, has analgesic potency 60-100 times that of morphine but is associated with respiratory depression and postoperative nausea and vomiting.[9] Ketamine causes release of norepinephrine, which can be blocked by barbiturates, droperidol, and benzodiazepines, which can cause a dose-dependent decrease in heart rate. The carotid sinus baroreceptor reflex of heart rate is markedly depressed by fentanyl.[10] It is also reported that, with propofol and ketamine, there is no decrease in the incidence of postoperative nausea and emesis, and there is no better recovery compared with the propofol and fentanyl combination.[11]

CONCLUSION

Presenting a comparative study, it is concluded that propofol-ketamine and propofol-fentanyl are equally safe and effective in total intravenous anesthesia for patients undergoing elective surgical procedures. Though there are variations in many parameters, clinically there is no significant difference. There is a slight increase HR and blood pressures (SBP&DBP) in the propofol-ketamine group after induction. In the propofol-fentanyl group, there is a slight reduction in systolic blood pressure after induction, so propofol-ketamine appears to have slightly better hemodynamic stability compared to the propofol-fentanyl group. Postoperative recovery is superior in the propofol-fentanyl group than in the propofol-ketamine group. The present study demands such clinical trials in a large number of patients at a hi-tech research center to confirm these significant findings.

Limitation of study: Owing to small number of patients we have limited findings and results.

- This research work was approved by GSL Medical College Rajahmandry, Andhra Pradesh-533296
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