Section: Anaesthesiology

Original Research Article

COMPARATIVE STUDY OF TWO DRUGS COMBINATION IN TOTAL INTRAVENOUS ANAESTHESIA - PROPOFOL AND KETAMINE AND PROPOFOL AND FENTANYL IN TELANGANA POPULATION

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Abstract

Background: Total intravenous anaesthesia (TIVA) is a technique where drugs are administered intravenously instead of volatile drugs. This TIVA technique provides rapid and complete recovery, making it suitable for day care surgeries with the fewest side effects. **Materials and Methods:** Out of 90 patients, 45 (Group-I) were administered propofol 1.0 mg/kg body weight and ketamine 1.0 mg/kg body weight as bolus dosage, and 45 (group-II) were given propofol 1.5 mg/kg body weight and fentanyl 0.2 mcg/kg body weight as bolus. At different stages (pre-induction, induction, intra-operative, post-operative stages), systolic BP, diastolic BP at different stages were compared and recorded. Moreover, post-operative side effects were also noted. **Results:** There was a significant p value in hemodynamic profile ($p<0.001$) during induction and intra-operative stages of anaesthesia but during post-operative stage of anaesthesia, systolic and diastolic BP were almost equal in both groups ($p>0.001$) with negligible post-operative side effects. **Conclusion:** In the present study, it was concluded that propofol, ketamine, and propofol, fentanyl were ideal alternatives to gaseous anaesthetic agents in elective surgeries.

INTRODUCTION

The purpose of general anaesthesia is to provide quick and pleasant induction, predictable loss of consciousness, stable operative conditions, minimal side effects, and rapid and smooth recovery of protective reflexes and psychomotor functions.[1]

In recent days, general anaesthesia (GA) has seen lots of advancements to benefit patients. Total intravenous anaesthesia (TIVA) is a technique where drugs are administered intravenously instead of volatile drugs. The benefit of TIVA is that it evades several shortcomings of inhalation anaesthesia while delivering rapid and painless recovery, in addition to a fewer incidence of post-operative nausea and vomiting, which makes it convenient for day care surgeries.[1] It is relatively less noxious, and it diminishes the malignant hyperthermia and environmental hazards, which include ozone depletion in the stratosphere.[2] When compared to inhalation anaesthesia TIVA has numerous benefits such as no operational room pollution, least cardiac depression, minor neuro-humoral response, and reduced oxygen consumption.[3]

The TIVA technique has become more popular because of its induction agents, amnestic agents, and opioids, as well as the advances in automated infusion pumps, including target controlled infusion systems (TCI) and syringe pumps.

A single drug can never deliver all properties; hence, various combinations of different drugs are advocated to get balance in TIVA.[4] This pragmatic study was aimed at comparing and evaluating the combination of two drug regimens, i.e., propofol-ketamine and propofol-fentanyl for TIVA, in terms of intra-operative and post-operative hemodynamic profile, post-operative recovery, and undesirable sequels of post-operative nausea and vomiting and other adverse side effects.

MATERIALS AND METHODS

90 patients admitted at surgery department of CMR Institute of Medical Sciences, Kandlakoya village, Medchal Road, Hyderabad-501401 were studied.

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Inclusive Criteria

Patients of ASA-I and ASA-II groups aged between 20 to 50 years, ready for elective surgery were selected for surgery.

Exclusion Criteria

Patients having history of allergy to particular drugs, allergy to fat or egg, pregnant females, patients on monoamine oxidise inhibitors, history of jaundice, age above 50 years of age, immuno compromised patients were excluded from study.

Method: As pre medication tablet Ranitidine 150 mg + Alprazolam 0.25mg were given a night before and 2 hour before the induction of surgery.

Anaesthesia technique – standard anaesthetic technique was used in every patient. After securing the intravenous line, monitoring gadgets were attached, which included an ECG, SpO2, and a non-invasive BP cuff. Baseline parameters were observed and recorded. Injection Midazolam (0.08 mg /kg with a maximum dose of 5 mg) was given I.V., 2 minutes before the induction of anaesthesia in both groups.

Induction of anaesthesia in patient Group-I was administered with Propofol 1.0mg/kg body weight and Ketamine 1.0 mg/kg body weight given as bolus dosages. Group-II was administered with Propofol 1.5 mg/kg body weight and Fentanyl 2.0 µg/kg body weight given as IV bolus doses.

In both groups, 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 a face mask for 60–90 seconds with the help of the Bains circuit and intubation was done with an appropriate size 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 anaesthesia: In group-I maintenance of anaesthesia was achieved with the infusion of propofol (1 mg/kg/h) and ketamine (2.0 mg/kg/h)while in group-II maintenance of anaesthesia was achieved with the infusion of propofol (2.0 mg/kg/h) and fentanyl (2.0 mcg/kg/h). Vecuronium bromide was used as a muscle relaxant at a dosage of 0.05–0.06 mg/kg body weight as an initial bolus dose and supplemented with top-ups of 1mg in both groups. Hemodynamic and other monitoring parameters were observed continuously and noted at an interval 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 anaesthesia drugs were stopped 5 minutes before the anticipated end of surgery. At the end of surgery, neuro-muscular blockade was reversed by injections of Neostigmine 40 µg/kg body weight and glycopyrrolate 10 µg/kg body weight, which were 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 post-operative side effects were compared with the z test and recorded. The statistical analysis was carried out using SPSS software. The ratio of males and females was 2:1.

RESULTS

Table 1: Comparison of mean pulse at different stages of anaesthesia in group-I and II

- Pre Induction – 84.04 (±5.14) in group-I, 84.15 (± 5.10) in group-II, t test was 0.73 and p>0.46 (p value is insignificant)
- Induction 1 Minute – 84.24 (±5.16) in group-I, 76.32 (± 4.48) in group-II, t test was 7.77 and p<0.001
- 2 Minute – 90.5 (±5.22) in group-I, 76.33 (± 4.36) in group-II, t test was 13.9 and p<0.001
- 3 Minute – 90.80 (±5.10) in group-I, 77.28 (± 4.32) in group-II, t test was 13.5 and p<0.001
- 4 Minute – 90.68 (±5.16) in group-I, 77.16 (± 4.25) in group-II, t test was 13.5 and p<0.001
- 5 Minute – 86.28 (±5.07) in group-I, 85.16 (± 4.30) in group-II, t test was 1.13 and p>0.2 (p value is insignificant)
- Intra-Operative period - 10 Minutes – 86.28 (±5.07) in group-I, 85.16 (±4.30) in group-II, t test was 1.13 and p>0.26 (p value is insignificant)
- At 20 Minutes – 84.48 (±5.28) in group-I, 88.04 (± 4.76) in group-II, t test was 3.35 and p<0.001
- At 30 Minutes – 84.28 (±5.04) in group-I, 87.65 (± 4.63) in group-II, t test was 3.30 and p<0.001
- At 40 Minutes – 84.89 (±5.18) in group-I, 87.88 (± 4.48) in group-II, t test was 2.92 and p<0.004
- At 50 Minutes – 84.56 (±5.05) in group-I, 87.06 (± 4.45) in group-II, t test was 2.49 and p<0.001
- At 60 Minutes – 84.25 (±5.04) in group-I, 67.32 (± 4.10) in group-II, t test was 4.10 and p<0.001
- Post-Operative group – at 1 Minute – 84.56 (±4.92) in group-I, 89.20 (± 3.96) in group-II, t test was 4.92 and p<0.001
- At 5 Minutes – 84.32 (±5.12) in group-I, 85.32 (± 4.04) in group-II, t test was 1.02 and p>0.30 (p value is insignificant)
- 10 Minutes – 84.24 (±5.24) in group-I, 84.77 (± 3.80) in group-II, t test was 0.05 and p>0.58 (p value is insignificant)
- 15 Minutes – 84.36 (±5.36) in group-I, 84.02 (± 4.08) in group-II, t test was 0.3 and p>0.7 (p value is insignificant)
- 20 Minutes – 84.56 (±5.42) in group-I, 89.12 (± 5.10) in group-II, t test was 4.11 and p<0.001

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

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- Pre-Induction – 125.92 (± 8.50) in group-I, 126.36 (± 9.65) in group-II, t test was 0.23 and p>0.81 (p value is insignificant)
- Induction- 1 Minute – 125.76 (±9.22) in group-I, 116.32 (± 9.46) in group-II, t test was 4.79 and p<0.001
- 2 Minute – 136.04 (±9.50) in group-I, 122.12 (± 9.28) in group-II, t test was 7.05 and p<0.001
- 3 Minute – 135.64 (±9.60) in group-I, 121.24 (± 9.23) in group-II, t test was 7.24 and p<0.001
- 4 Minute – 132.04 (±9.64) in group-I, 121.05 (± 9.34) in group-II, t test was 5.48 and p<0.001
- 5 Minute – 130.24 (±9.45) in group-I, 120.16 (± 9.23) in group-II, t test was 5.12 and p<0.001
- Intra-Operative group – At 10 Minutes – 129.72 (±9.38) in group-I, 126.16 (± 9.78) in group-II, t test was 1.76 and p>0.008
- At 20 Minutes – 128.62 (±9.68) in group-I, 130.20 (± 9.10) in group-II, t test was 0.79 and p>0.004
- At 30 Minutes – 128.18 (±9.70) in group-I, 132.04 (± 8.58) in group-II, t test was 1.99 and p>0.004
- At 40 Minutes – 128.04 (±9.82) in group-I, 130.22 (± 8.42) in group-II, t test was 1.13 and p>0.26
- 50 Minutes – 127.88 (±6.33) in group-I, 132.06 (± 8.52) in group-II, t test was 3.27 and p>0.01
- Post-Operative group – At 1 Minute – 132.20 (±9.58) in group-I, 136.13 (± 8.52) in group-II, t test was 2.05 and p<0.004
- At 5 Minutes – 128.35 (±9.72) in group-I, 128.30 (± 9.22) in group-II, t test was 0.02 and p>0.98
- At 10 Minutes – 128.24 (±9.66) in group-I, 126.26 (± 9.13) in group-II, t test was 0.99 and p>0.32
- At 15 Minutes – 128.04 (±9.50) in group-I, 125.18 (± 9.22) in group-II, t test was 1.44 and p>0.15
- At 20 Minutes – 127.79 (±9.57) in group-I, 123 (± 6.4) in group-II, t test was 2.40 and p<0.001

Table-3: Comparison of diastolic blood pressure in both groups at different stages of Anaesthesia

- Pre-Induction – 80.54 (±3.56) in group-I, 80.09 (± 3.54) in group-II, t test was 0.60 and p>0.54
- Induction- At 1st Minute – 80.40 (±3.52) in group-I, 73.60 (± 3.62) in group-II, t test was 9.03 and p<0.001
- 2nd Minute – 86.24 (±3.74) in group-I, 75.72 (± 3.52) in group-II, t test was 13.7 and p<0.001
- 3rd Minute – 86.67 (±3.86) in group-I, 75.48 (± 3.42) in group-II, t test was 14.5 and p<0.001
- 4th Minute – 86.44 (±3.73) in group-I, 75.32 (± 3.54) in group-II, t test was 14.5 and p<0.001
- 5th Minute – 86.92 (±3.54) in group-I, 75.20 (± 3.48) in group-II, t test was 15.8 and p<0.001
- Intra-Operative group – 10th Minutes – 81.84 (±3.62) in group-I, 81.12 (± 3.52) in group-II, t test was 0.95 and p>0.34 (p value is insignificant)
- 20th Minutes – 81.32 (±3.97) in group-I, 83.44 (± 3.52) in group-II, t test was 2.68 and p<0.001
- 30th Minutes – 81.28 (±3.95) in group-I, 84.44 (± 3.52) in group-II, t test was 4.07 and p<0.002
- 40th Minutes – 81.44 (±4.04) in group-I, 83.44 (± 3.57) in group-II, t test was 3.11 and p<0.002
- 50th Minutes –81.36 (±4.32) in group-I, 84.84 (± 3.38) in group-II, t test was 4.25 and p<0.001
- 60 Minutes –81.52 (±3.92) in group-I, 85.24 (± 3.32) in group-II, t test was 4.85 and p<0.001
- Post-Operative group - 1 Minute – 82.04 (±4.02) in group-I, 86.36 (± 4.11) in group-II, t test was 5.02 and p<0.001
- 5th Minutes – 79.13 (±3.84) in group-I, 80.87 (± 4.14) in group-II, t test was 2.05 and p<0.04
- 15th Minutes – 78.60 (±4.32) in group-I, 78.80 (± 3.04) in group-II, t test was 2.25 and p>0.80 (p value is insignificant)
- 20th Minutes – 78.56 (±4.21) in group-I, 79.78 (± 3.52) in group-II, t test was 1.49 and p>0.14 (p value is insignificant)

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

- At 5 Minutes – 0.46 (±0.6) in group-I, 0.67 (± 0.8) in group-II, t test was 1.40 and p>0.016
- At 10 Minutes – 0.82 (±0.6) in group-I, 1.08 (± 0.4) in group-II, t test was 2.41 and p<0.001
- At 15 Minutes – 1.72 (±0.6) in group-I, 1.74 (± 0.5) in group-II, t test was 0.17 and p>0.86 (p value is insignificant)
- At 20 Minutes – 1.98 (±0.4) in group-I, 2.04 (± 0.5) in group-II, t test was 0.62 and p>0.53 (p value is insignificant)

Table-5: Comparison of post-operative side effects

- Nausea – 1 (2.22%) in group-I, 3 (6.66%) in group-II
- Secretions 4 (8.88%) in group-I,.

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

Anaesthesia stage	Time Interval	Group	Mean SD	t test	p value
Pre-Induction	--	I=45 II=45	84.04 (±85.14) 84.15 (±5.0)	0.13	p>0.46
Induction	1 Min	I II	84.24 (±5.16) 76.32 (±4.48)	7.77	P<0.001
	2 Min	I II	90.5 (±5.22) 76.33 (±4.36)	13.9	P<0.001
	3 Min	I II	90.80 (±5.10) 77.28 (±4.32)	13.5	P<0.001
	4 Min	I II	90.68 (±5.16) 77.16 (±4.25)	13.5	P<0.001

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	5 Min	I II	86.28 (±5.079) 85.16 (±4.30)	1.13	P>0.26
Intra-Operative	10 Min	I II	86.28 (±5.07) 85.16 (±4.30)	1.13	P>0.26
	20 Min	I II	84.48 (±5.28) 88.04 (±4.70)	3.35	P<0.001
	30 Min	I II	84.28 (±5.04) 87.65 (±4.63)	3.30	P<0.001
	40 Min	I II	84.89 (±5.18) 87.88 (±4.48)	2.92	P<0.004
	50 Min	I II	84.56 (±5.05) 87.06 (±4.45)	2.49	P<0.001
	60 Min	I II	84.25 (±5.04) 67.32 (±4.10)	17.4	P<0.001
Post-Operative	1 Min	I II	84.56 (±4.92) 89.20 (±3.98)	4.92	P<0.001
	5 Min	I II	84.32 (±5.12) 85.32 (±4.04)	1.02	P>0.36
	10 Min	I II	84.24 (±5.24) 84.77 (±3.80)	0.5	P>0.58
	15 Min	I II	84.36 (±5.36) 84.02 (±4.80)	0.3	p>0.7
	20 Min	I II	84.56 (±5.42) 89.12 (±5.10)	4.11	P<0.001

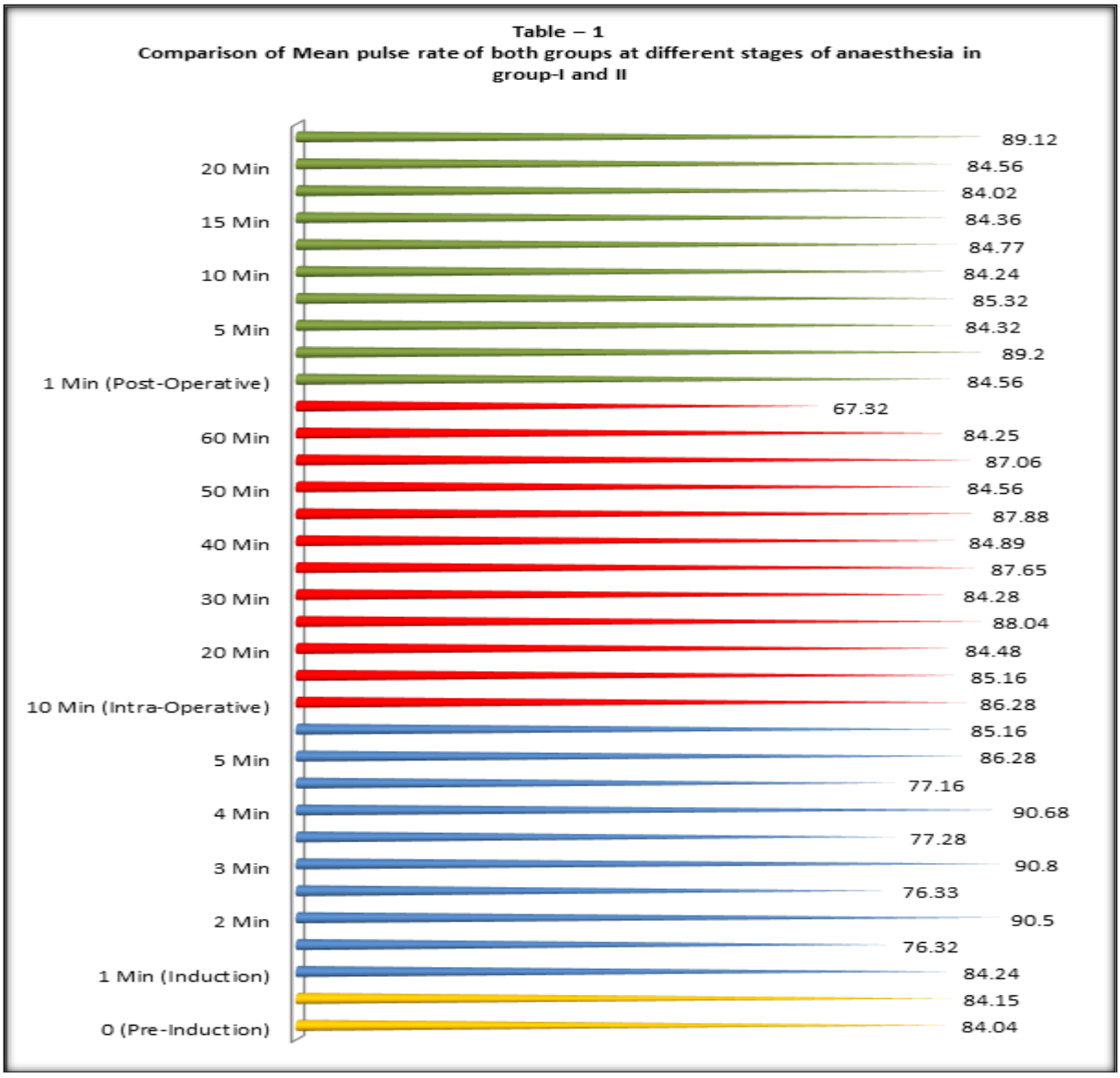

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Table 2: Comparison of systolic Blood pressure in both groups at different stages of anaesthesia

Anaesthesia stage	Time Interval	Group	Mean SD	t test	p value
Pre-Induction	--	I II	125.92 (±9.50) 126.36 (±9.66)	0.23	p>0.81
Induction	1 Min	I II	125.76 (±9.22) 116.32 (±9.46)	4.79	P<0.001
	2 Min	I II	136.04 (±9.50) 122.12 (±9.28)	7.03	P<0.001
	3 Min	I II	135.64 (±9.60) 121.24 (±9.23)	7.24	P<0.001
	4 Min	I II	132-04 (±9.64) 121.05 (±9.38)	5.48	P<0.001
	5 Min	I II	130.24 (±9.43) 120.16 (±9.23)	5.12	P<0.001
Intra-Operative	10 Min	I II	129.72 (±9.38) 126.16 (±9.78)	1.76	P>0.08
	20 Min	I II	128.62 (±9.68) 130.20 (±9.10)	0.79	P>0.42
	30 Min	I II	128.18 (±9.70) 132.04 (±8.58)	1.99	P>0.04
	40 Min	I II	128.04 (±9.82) 130.22 (±8.42)	1.13	P>0.26
	50 Min	I II	127.88 (±6.35) 132.06 (±8.52)	3.27	P>0.001
Post-Operative	1 Min	I II	132.20 (±9.58) 136.13 (±8.52)	2.05	P<0.04
	5 Min	I II	128.35 (±9.72) 128.30 (±9.22)	0.02	p>0.98
	10 Min	I II	128.24 (±9.66) 126.26 (±9.13)	0.99	p>0.32
	15 Min	I II	128.04 (±9.50) 125.18 (±9.22)	1.44	p>0.15
	20 Min	I II	127.79 (±9.57) 123.65 (±6.26)	2.42	P<0.01

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	80.54 (±3.56) 80.09 (±3.54)	0.60	p>0.54
Induction	1 Min	I II	80.40 (±3.52) 73.60 (±3.62)	9.03	P<0.001
	2 Min	I II	86.24 (±3.74) 75.72 (±3.52)	13.7	P<0.001
	3 Min	I II	86.67 (±3.86) 75.48 (±3.42)	14.5	P<0.001
	4 Min	I II	86.44 (±3.73) 75.32 (±3.54)	14.5	P<0.001
	5 Min	I II	86.92 (±3.62) 75.20 (±3.42)	15.8	P<0.001
Intra-Operative	10 Min	I II	81.84 (±3.62) 81.12 (±3.52)	0.95	p>0.34
	20 Min	I II	81.32 (±3.97) 83.44 (±3.52)	2.68	P<0.001
	30 Min	I II	81.28 (±3.95) 84.44 (±3.52)	4.07	P<0.002
	40 Min	I II	81.44 (±4.04) 83.94 (±3.57)	3.11	P<0.002
	50 Min	I II	81.36 (±4.32) 84.84 (±3.38)	4.25	P<0.001
	60 Min	I II	81.52 (±3.92) 85.24 (±3.32)	4.85	P<0.001
Post-Operative	1 Min	I II	82.04 (±4.04) 86.36 (±4.17)	5.02	P<0.001
	5 Min	I II	79.13 (±3.84) 80.87 (±4.17)	2.05	p>0.04
	15 Min	I II	78.60 (±4.32) 79.80 (±3.04)	0.25	p>0.80
	20 Min	I II	78.56 (±4.21) 79.78 (±3.52)	1.49	p>0.14

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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	0.46 (± 0.6) 0.67 (±0.8)	1.40	P>0.16
10 Minutes	I II	0.82 (±0.6) 1.08 (±0.4)	2.41	P<0.001
15 Minutes	I II	1.72 (±0.6) 1.74 (±0.5)	0.17	p>0.85
20 Minutes	I II	1.98 (±0.4) 2.04 (±0.5)	0.62	p>0.53

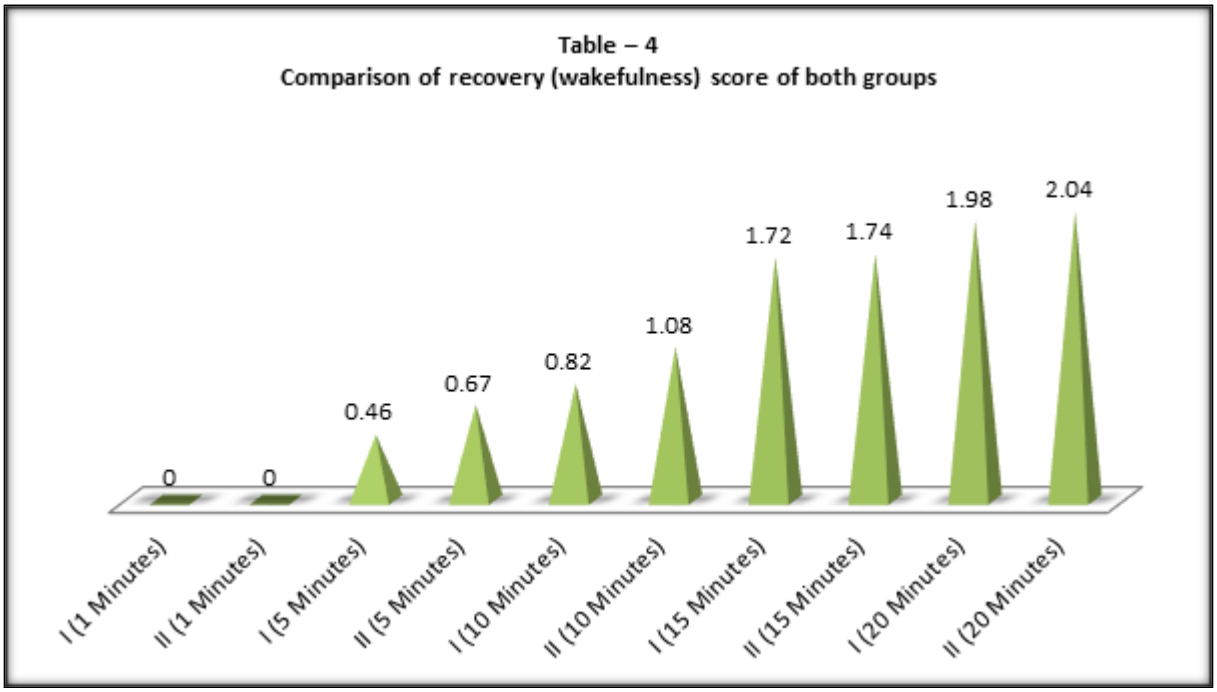

Table 5: Comparison of post-operative side effects

Side effects	Group-I No	Percentage (%)	Group-II No	Percentage (%)
Nausea	1	2.22	3	6.66
Vomiting	-	-	-	-
Secretions	4	8.88	-	-
Laryngospasm/ Bronchospasm	-	-	-	-
Post-ketamine sequelae	-	-	-	-
Excretion	-	-	-	-
Hallucination	-	-	-	-
Euphoria	-	-	-	-

DISCUSSION

Aim is to present a comparative study of two drug combinations of TIVA- propofol and ketamine, propofol and fentanyl, in the Telangana population. In comparison of the mean pulse rate of both groups at different stages of anaesthesia, induction stages of 1, 2, 3, and 4 minutes were highly significant (p<0.001), intraoperative 20, 30, 40 and 50 minutes had a significant p value (p<0.001), post-operative 1 minute and 20 minutes were highly significant (p<0.001) (Table-1). In a comparative study of systolic blood pressure, in the pre induction period 1, 2, 3, 4, 5 min timings had a significant p value (p<0.001) but in the intraoperative period, both values were similar and p values were insignificant (p<0.001). Post-operatively, except for the 1 minute duration, all values are similar, hence the p value is insignificant (p>0.001)(Table-2) In comparison of diastolic blood pressure, 1, 2, 3, 4, 5, 20, 30, 40, 50, 60 minutes intervals had significant p values (p<0.001), post-operatively, 1, 5 minutes intervals had significant p values (p<0.0010) and the remaining intervals had similar values, but the p value was insufficient (p>0.001) (Table-3) In comparison, the recovery (wakefulness) score of both groups at 5, 10, 20 minutes intervals had a significant p value (p<0.001) (Table-4). In the comparison study of post-operative side effects,

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nausea was observed in 1 (2.22%) in group-I and in 3 (6.66%) in group-II, secretions were observed in 4 (8.88%) in group-I only (Table-5). These findings are more or less in agreement with previous studies.[5,6,7]

Anaesthesia is seldom accomplished by a single drug because no single drug is able to provide all components of anaesthesia without seriously compromising hemodynamic and/or respiratory function, reducing operating conditions or delaying post-operative recovery. Because of small therapeutic window, a detailed characterization of the concentration effect relationships of anaesthetic 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.

The availability of rapid and short acting sedative hypnotics, analgesics and muscle relaxants has refocussed the attention in complete anaesthesia by intravenous route. The advent of continuous infusion system has made TIVA more popular and convenient. Propofol is substitute phenol derivative which is associated with rapid smooth induction, good maintenance and rapid recovery.[8] Ketamine is a potent analgesic which has high margin of safety. It produces no negative influence on ventilation or circulation. Its main disadvantage is emergence delirium. Fentanyl, a phenyl peperidine derivative has analgesic potency 60-100 times that of morphine, but is associated with respiratory depression and post-operative nausea and vomiting.[9]

Ketamine causes release of norephinephrine which can be blocked by Barbiturates, Droperidol and Benzodiazepine which can cause dose dependent decrease in heart rate. Carotid sinus baroreceptor reflex of heart rate is markedly depressed by Fentanyl.[10] It is also reported that, in propofol, ketamine combination there is no decrease in the incidence of post-operative nausea or emesis and there is no better recovery compared with propofol, fentanyl combination.[11]

CONCLUSION

In the present comparative study, it is concluded that, propofol, ketamine, and fentanyl are equally safe and effective in total intravenous anaesthesia for patients undergoing elective surgical procedures. Though there is a significant difference in many parameters, clinically, there is no significant difference. There is a slight increase in systolic blood pressure in propofol and the ketamine group after induction. In the propofol plus fentanyl group, there is a slight reduction in systolic blood pressure after induction, so propofol and ketamine combination appears to have slightly better hemodynamic stability compared to the propofol plus fentanyl combination. Post-operative 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 centre to confirm these significant findings.

Limitation of study

Owing to the tertiary location of the research centre, the small number of patients, and the lack of the latest techniques, we have limited findings and research.

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