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Original Research Article

Comparative Study of Two Drugs Combination in Total Intravenous Anaesthesia - Propofol and Ketamine, Propofol and Fentanyl

Piyush Bhalchandra Wani[1], Shivraj N Chilwant[2]

[1]Associate Professor, K. J. Somaiya Medical College and Research centre, Mumbai, Maharashtra-400012.
[2]Assistant Professor, Department of Anaesthesia, Prakash Institute of Medical Sciences, Uran Islampur, Maharashtra-415409

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Corresponding Author: Dr. Shivraj N Chilwant
Conflict of interest: Nil

Abstract:

Background: Total intravenous anaesthesia (TIVA) is a genuine technique of ideal drug combination usually used in general anaesthesia. It has minimum cardiac depression, a lesser neuro-humeral response and decreased oxygen consumption. Hence, it is proven to be an ideal technique.

Method: 100 (one hundred) patients were classified 50 in group-I, 50 in group-II, Group I was administered Propofol 1.0 mg/kg body weight, Ketamine 1.0 mg/kg body weight as bolus dosage and group-II was given Propofol 1.0 mg/kg body weight and Fentanyl 2mcg/kg body weight as a bolus. At different stages (pre-induction, induction, intra-operative, and post-operative anaesthesia), different stages were compared, and significant results were noted. Moreover, post-operative side effects were also noted.

Results: There was a significant p value in the induction stage, intra-operative stages of anaesthesia, and hemodynamic profile had a significant p value ($p<0.001$), but in the post-operative stages of anaesthesia, systolic and diastolic P were almost equal in both groups, hence the p value was insignificant ($p > 0.001$). It had negligible post-operative side effects.

Conclusion: It is concluded that Propofol, Ketamine, and Fentanyl are ideal alternatives to gaseous anaesthetic agents in elective surgeries because TIVA has the fewest side effects because of minimal cardiac depression.

Keywords: Total Intravenous Anaesthesia (TIVA), Propofol, Ketamine, Neostigmine, Glycopyrrolate.

Introduction

The main purpose of general anaesthesia is to provide quick and pleasant induction, predictable loss of consciousness, stable operative conditions with minimal side effects and rapid, smooth recovery of protective reflexes and psychomotor functions [1]
General anaesthesia has undergone a vast number of improvements and modifications and even the recently modified form of total intravenous anaesthesia (TIVA induction as well as maintenance of anaesthesia with intravenous agents only) has undergone many important changes since its introduction into clinical practice [2].

Previously, inhalational agents have remained the choice for maintaining anaesthesia. Monitoring the system that permits nearly accurate measurement of the endtidal concentration of volatile anaesthetics as well as the introduction of new potent volatile agents, provides a wider choice of drugs [3]. Inhalation agents have certain drawbacks and shortcomings. These include cost factors, different specific vaporizers require repeated maintenance, a scavenging system is mandatory, otherwise there will be pollution in the operation room environment, which is a big hazard [4]. But TIVA has many advantages like no operating room pollution, minimal cardiac depression, a lesser neuro-humoral response, decreased oxygen consumption, postoperative diffusion hypoxemia and decreased postoperative nausea and vomiting in day-care surgery. Hence, an attempt is made to use the TIVA technique to find drug combinations that can be used in general anaesthesia and compare them in both groups to justify the ideal group of TIVA.

Material and Method

100 (one hundred) patients admitted to the surgery department of K. J. Somaiya Medical College and Research Centre, Mumbai, Maharashtra-400012, were studied.

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

Exclusion Criteria: Patients with a history of allergy to particular drugs, allergies to fat or eggs,

pregnant females, patients on monoamine oxidase inhibitors, a history of jaundice, an age above 50 years of age, or immune compromised patients were excluded from the study.

Method:

As pre-medication tablets, Ranitidine 150 mg and Alprazolam 0.25mg were given a night before and 2 hours before the induction of surgery.

Anaesthesia technique: The 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 0.02 mg/kg 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 1.0 mg/kg body weight and Ketamine 1.0 mg/kg body weight given as bolus dosages. Group-II was administered Propofol 1.0 mg/kg body weight and Fentanyl 2.0 µg/kg body weight given as IV bolus doses. Hemodynamics 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).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 on spontaneous respiration.

The duration of study was February 2022 to February 2023

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.

Observation and Results

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

- **Pre-induction:** group-I, 84.20 (±6.12), group-II, 84.14 (± 5.12), t test was 0.16 and p>0.01 (p value is insignificant).
- **Induction** 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, and 30 minutes have highly significant p values (p<0.001).
- **Intra-operative Stage:** 50 minutes, 60 minutes have a significant p value (p<0.001).
- **Post-Operative Stage:** 1 minute, 20 minutes have a significant p value (p<0.01).

Table 2: Comparative Study of Systolic Blood Pressure in Both Groups

- **In pre-induction,** 125.90 (± 8.48) in group I and 126.34 (± 9.64) in group II, the t test was 0.23, and the p value is insignificant.
- **In the induction stage, 1** minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, and 10 minutes have significant p values (p<0.001).
- **Intra-operative group:** 30 minutes, 50 minutes have a significant p value (p<0.001).
- **Post-operative group:** 1 minute, 5 minutes only have a significant p value (p<0.001).

Table 3: Comparative study of diastolic blood pressure in both groups at different stages of anaesthesia

- **Pre-Induction:** 80.52 (±3.54) in group I, 80.07 (± 3.52) in group II, t test was 0.63, and p value was insignificant.
- **Induction Stage:** 1 minute, 2 minutes, 3 minutes, 4 minutes, and 5 minutes have a significant p value (p<0.001).
- **Intra-operative group:** 20 minutes, 30 minutes, 40 minutes, 50 minutes, and 60 minutes have a significant p value.
- **In the post-operative stage,** at 1 minute and 5 minutes, there is a significant p value (p<0.001).

Table 4: Comparative study of recovery (wakefulness score) scores of both groups At 10 minutes, only significant (p¬<0.001)

Table 5: Comparative study of post-operative side effects

- Nausea: 1 (2%) in group I, 3 (6%) in group II
- Secretions 4 (8%) were observed only 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=50 II=50	84.02 (±6.12) 84.14 (±5.2)	0.16	p>0.91
Induction	1 Min	I=50 II=50	84.22 (±5.15) 76.36 (±4.46)	8.18	P<0.001
	2 Min	I=50 II=50	84.22 (±5.14) 76.30 (±4.50)	13.2	P<0.001
	3 Min	I II	90.78 (±5.8) 77.26 (±4.32)	13.2	P<0.001
	4 Min	I II	90.66 (±5.14) 77.14 (±4.23)	14.3	P<0.001
	5 Min	I II	86.26 (±5.09) 85.14 (±4.28)	1.19	P>0.23
Intra-Operative	10 Min	I II	86.26 (±5.05) 85.14 (±4.28)	1.19	P>0.23
	20 Min	I II	84.46 (±5.26) 88.46 (±4.68)	4.02	P<0.002
	30 Min	I II	84.26 (±4.05) 87.64 (±3.60)	4.41	P<0.001
	40 Min	I II	84.87 (±5.16) 87.86 (±4.46)	3.12	P<0.002
	50 Min	I II	84.55 (±5.04) 87.04 (±4.41)	2.62	P<0.001
	60 Min	I II	84.24 (±5.02) 67.30 (±4.08)	18.5	P<0.001
Post-Operative	1 Min	I II	84.54 (±4.90) 89.18 (±3.96)	5.20	P<0.001
	5 Min	I II	84.30 (±5.10) 85.30 (±4.02)	1.08	P>0.27
	10 Min	I II	84.22 (±5.22) 84.75 (±3.70)	0.58	P>0.58
	15 Min	I II	84.34 (±5.35) 84.04 (±4.78)	0.29	p>0.76
	20 Min	I II	84.54 (±5.40) 89.10 (±5.12)	4.33	P<0.001

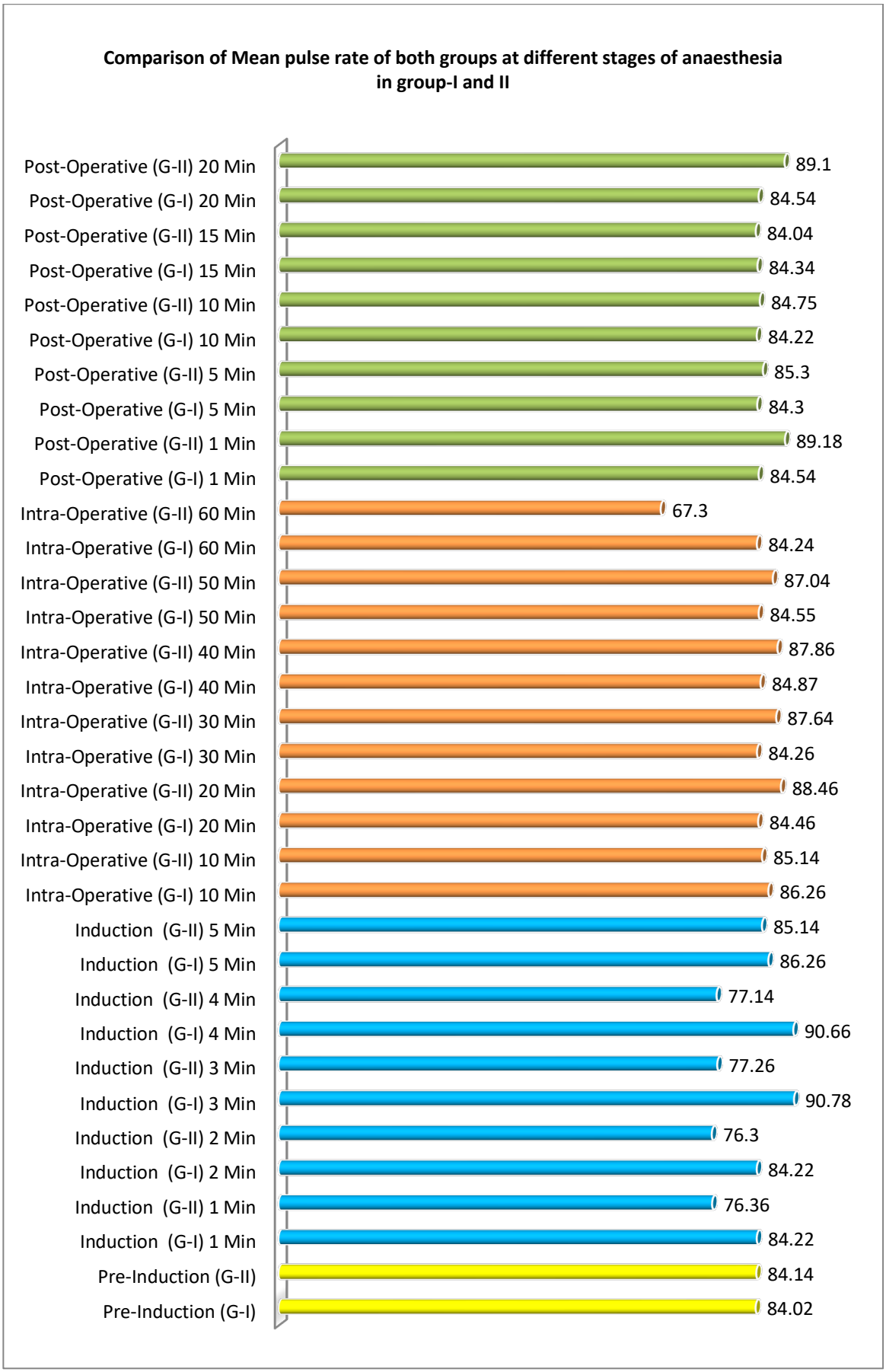

Figure 1: Comparison of Mean pulse rate of both groups at different stages of anaesthesia in group-I and II

Table 2: Comparative study 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=50 II=50	125.90 (±9.48) 126.34 (±9.64)	0.23	p>0.81
Induction	1 Min	I II	125.75 (±9.20) 116.30 (±9.44)	5.06	P<0.001
	2 Min	I II	136.06 (±9.48) 122.10 (±9.26)	7.44	P<0.001
	3 Min	I II	135.62 (±9.58) 121.22 (±9.20)	7.66	P<0.001
	4 Min	I II	132-02 (±9.62) 121.04 (±9.36)	6.73	P<0.001
	5 Min	I II	130.22 (±9.42) 120.14 (±9.20)	5.41	P<0.001
Intra-Operative	10 Min	I II	129.70 (±4.36) 126.14 (±9.76)	2.35	P>0.02
	20 Min	I II	128.60 (±9.66) 130.18 (±9.8)	0.81	P>0.41
	30 Min	I II	128.16 (±9.68) 132.06 (±8.56)	2.13	P>0.03
	40 Min	I II	128.06 (±9.80) 130.20 (±8.40)	1.12	P>0.24
	50 Min	I II	127.86 (±6.33) 132.04 (±8.50)	2.78	P>0.001
Post-Operative	1 Min	I II	132.22 (±9.50) 136.11 (±8.50)	2.15	P<0.01
	5 Min	I II	128.33 (±9.70) 128.28 (±9.20)	0.03	p>0.97
	10 Min	I II	128.22 (±9.64) 126.24 (±9.11)	1.05	p>0.29
	15 Min	I II	128.06 (±9.48) 125.16 (±9.20)	1.55	p>0.12
	20 Min	I II	127.77 (±9.55) 123.62 (±6.24)	2.55	P>0.12

Table 3: Comparative study 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=50 II=50	80.52 (±3.54) 80.07 (±3.52)	0.63	p>0.52
Induction	1 Min	I II	80.38 (±3.50) 73.58 (±3.60)	9.59	P<0.001
	2 Min	I II	86.22 (±3.72) 75.70 (±3.50)	14.5	P<0.001
	3 Min	I II	86.65 (±3.84) 75.46 (±3.40)	15.4	P<0.001
	4 Min	I II	86.42 (±3.70) 75.30 (±3.52)	15.3	P<0.001
	5 Min	I II	86.90 (±3.60) 75.18 (±3.40)	16.7	P<0.001
Intra-Operative	10 Min	I II	81.82 (±3.60) 81.10 (±3.50)	1.01	p>0.31
	20 Min	I II	81.30 (±3.95) 83.42 (±3.50)	2.64	P<0.001
	30 Min	I II	81.26 (±3.94) 84.42 (±3.50)	4.24	P<0.001
	40 Min	I II	81.42 (±4.02) 83.92 (±3.55)	3.29	P<0.001
	50 Min	I II	81.34 (±4.30) 84.92 (±3.35)	3.29	P<0.001

	60 Min	I II	81.50 (±3.90) 85.22 (±3.30)	5.08	P<0.001
Post-Operative	1 Min	I II	82.02 (±4.02) 86.34 (±4.15)	5.28	P<0.001
	5 Min	I II	79.11 (±3.82) 80.85 (±4.15)	2.18	p>0.03
	15 Min	I II	78.58 (±4.30) 79.82 (±3.02)	1.66	p>0.09
	20 Min	I II	78.54 (±4.12) 79.76 (±3.50)	1.58	p>0.11

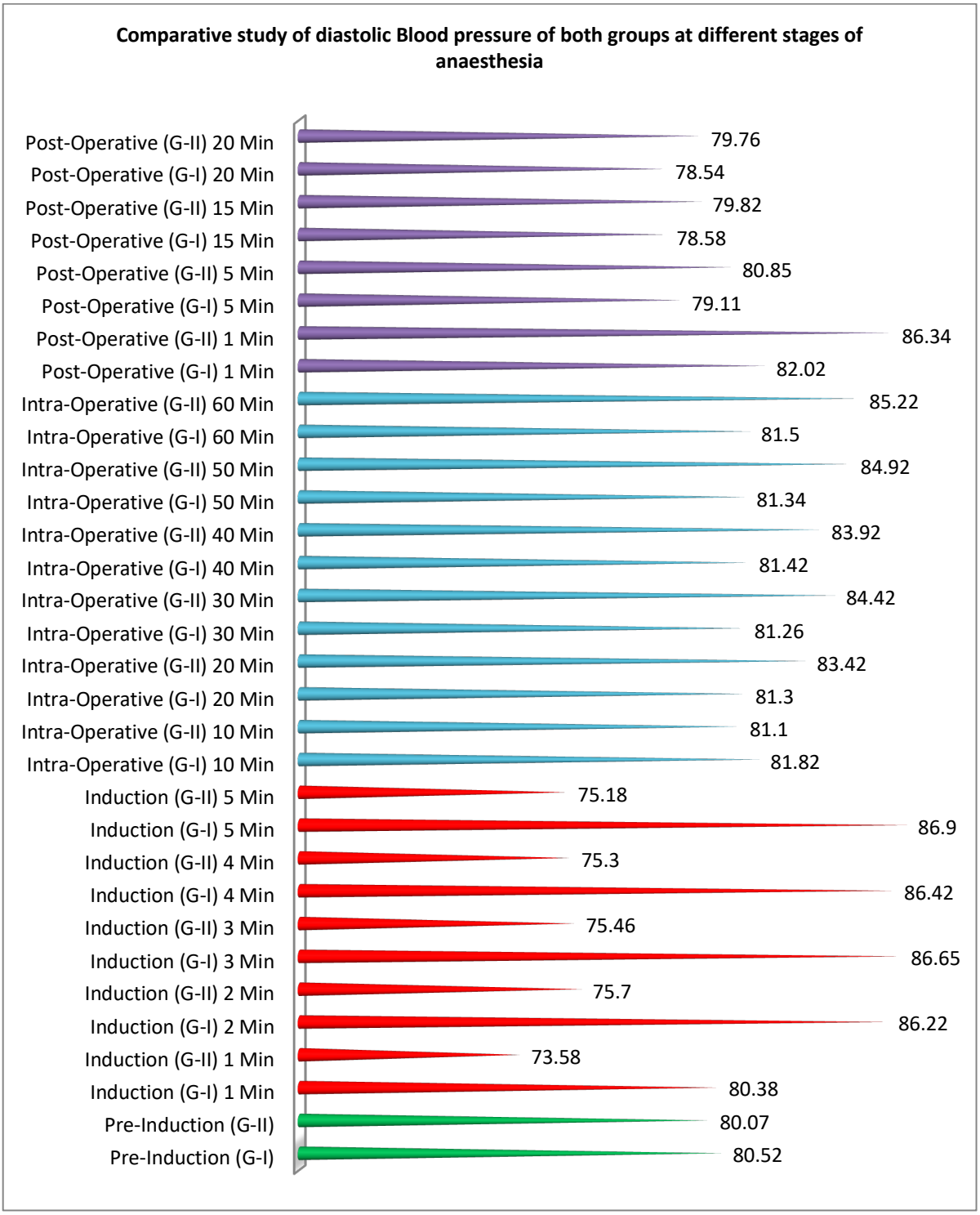

Figure 2: Comparative study of diastolic Blood pressure of both groups at different stages of anaesthesia

Table 4: Comparative study of recovery (wakefulness) score of both groups

Time Interval	Group	Mean (±SD)	t test	p value
1 Minutes	I=50 II=50	--	--	--
5 Minutes	I II	0.45 (± 0.5) 0.68 (±0.9)	1.58	P>0.12
10 Minutes	I II	0.80 (±0.8) 1.10 (±0.5)	2.24	P<0.002
15 Minutes	I II	1.70 (±0.4) 1.72 (±0.6)	0.19	p>0.84
20 Minutes	I II	1.96 (±0.2) 2.06 (±0.65)	1.11	p>0.26

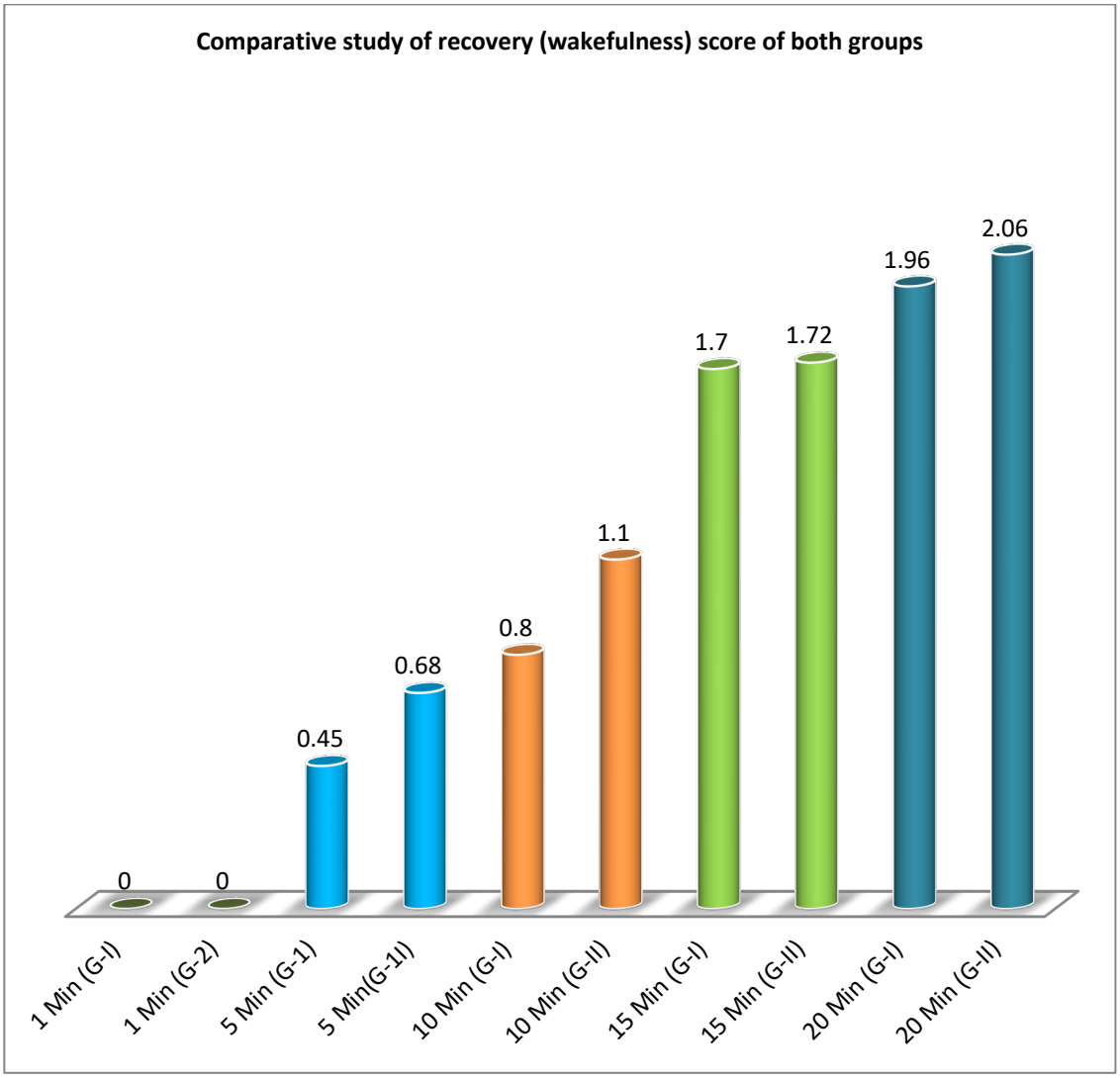

Figure 3: Comparative study of recovery (wakefulness) score of both groups

Table 5: Comparison of post-operative side effects

Side effects	Group-I (50)	Percentage (%)	Group-II No	Percentage (%)
Nausea	1	2%	3	6%
Vomiting	-	-	-	-
Secretions	4	8%	-	-
Laryngospasm/ Bronchospasm	-	-	-	-
Post-ketamine squeal	-	-	-	-
Excretion	-	-	-	-
Hallucination	-	-	-	-
Euphoria	-	-	-	-

Discussion

Present a comparative study of two drug combinations in the total intravenous anaesthesia propofol and ketamine and propofol and fentanyl. Comparison of mean pulse rates in both groups at different stages of anaesthesia. In induction stages, 1 minute, 2 minutes, 3 minutes, 4 minutes, 20 minutes, and 30 minutes have a significant p value ($p<0.001$). In the intra-operative stage, there is a significant p value ($p<0.001$). In post-operative care, both groups have similar pulse rates (Table 1). In comparison to systolic BP in both groups, the induction stage has a significant p value ($p<0.001$). During the intra-operative stage, at 50 minutes, gas had a significant p value ($p<0.001$). In the postoperative period, systolic BP is stable in both groups (Table 2). In the comparative study of diastolic BP induction stage, there was a significant p value ($p<0.001$), but in the intra-operative period and postoperative stage, systolic BP remained stable in both groups (Table 3). In the comparison study recovery (wakefulness) score both groups have same score (Table-4). In the comparison of post-operative side effects, group 1 (2%) had one patient have nausea, and group 3 (6%) had nausea, and secretion was 4 (8%) (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 the small therapeutic window, a detailed characterization of the concentration-effect relationships of anaesthetics 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 has refocused attention on complete anaesthesia by intravenous route. The advent of continuous infusion systems has made TIVA more popular and convenient. Propofol is a substitute phenol derivative that 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 the emergence of 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 the release of nor-ephinephrine, which can be blocked by barbiturates, droperidol, and benzodiazepine, which can cause a dose-dependent decrease in heart rate. The carotid sinus baro-receptor reflex of heart rate is markedly depressed by fentanyl [10]. It is also reported that in the propofol-ketamine combination, there is no decrease in the incidence of post-operative nausea or emesis, and there is no better recovery compared with the propofol-fentanyl combination [11].

Summary and 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 the 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 that, such clinical trials must be conducted in a large number of patients at a hi-tech research centre to confirm these significant findings.

Limitation of study: Small number of patients and the lack of the latest techniques, we have limited findings and results.

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