

A Comparative Study of Ketamine-Propofol versus Fentanyl-Propofol in Total Intravenous Anaesthesia- A Double Blind Randomised Clinical Trial

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Abstract: ***Background:** Propofol has emerged as a gold-standard for total intravenous anaesthesia (TIVA) for short surgical interventions but lack of analgesia remains its main shortcoming, therefore it is always combined with an analgesic. Ketamine and fentanyl are the popular analgesic in this context. This study was carried out to compare these drugs with propofol to assess haemodynamic and recovery profile of either combination. **Objective:** To evaluate quality and compare haemodynamic variability of anaesthesia among the patients scheduled for short surgical procedures in ketamine-propofol and fentanyl-propofol groups. **Materials and Methods :** In this study, 60 consenting patients undergoing short elective surgeries were divided into two groups of fifty each. Group PF received propofol 2.5 mg/kg + fentanyl 1µg/kg for induction and propofol 2 mg/kg/hr. + fentanyl 0.5µg/kg/hr for maintenance of anaesthesia and group PK received propofol 2.5 mg/kg + ketamine 1 mg/kg for induction and propofol 2 mg/kg/hr. + ketamine 1 mg/kg/hr. for maintenance of anaesthesia. Haemodynamic variables were recorded pre, intra and postoperatively at regular intervals. At the end of drug infusion(s), time to spontaneous eye opening and response to postoperative questionnaire was noted to assess recovery. All the data presented as mean + standard deviation. **Results:** Patients in both groups did not differ significantly in demographic profile and haemodynamic parameters. Time to spontaneous eye opening was similarly comparable in both the groups (8 ± 3 min. and 8 ± 2 min.) (p = 0.53). Response to postoperative questionnaire at 30 minutes after anaesthesia was good in both the groups. Incidence of postoperative nausea and vomiting was also statistically insignificant between both the groups. (p = 0.74). **Conclusion:** Ketamine and fentanyl with propofol infusion for short surgical procedures are equally safe and efficacious. In both groups stable haemodynamics and good recovery profile were noted.*

Keywords: Total Intravenous Anaesthesia, Ketamine, Propofol, Fentanyl

1. Introduction

Total intravenous anaesthesia (TIVA)¹ is defined as a technique of anaesthesia which involves use of intravenous drugs to anaesthetise the patient without the use of inhalational agents. The concept of intravenous (IV) anaesthesia has progressed over a period of time from induction of general anaesthesia to modern day (TIVA) largely due to the better understanding of drug kinetics and dynamics along with the development of intravenous drug delivery systems that are able to titrate and deliver accurately the infusion dose of a given intravenous agent. New concepts in pharmacokinetic modeling coupled with advances in the technology of infusion pumps which allow the use of algorithms such as Target Controlled Infusion can be given via TIVA. It was Sigismund Elsholtz who first attempted intravenous anaesthesia in 1665. In fact, chloral hydrate² was the first anaesthetic agent to be introduced intravenously way back in 1870. Real advance in intravenous anaesthesia took place during 1921 when Daniel and Gabriel² Bardet published their experiences using somnifaine. Fredet and Perlis combined somnifaine with subcutaneous injection of morphine to supplement the effects of somnifaine. To begin with a Vann's 10 mL syringe was used for this purpose. To facilitate continuous intravenous infusion Abel's syringe 3 was used. Of all the intravenous anaesthetic agents that are available, Propofol's pharmacokinetic profiles favour administration by continuous intravenous infusion.^{3,4,5} As Propofol has very little nociceptive effect, it is generally combined with an analgesic, the popular combination being either Propofol with Fentanyl or Propofol with Ketamine. Pain relief to patient is an important constituent of balanced anaesthesia. Ketamine is a potent analgesic; its anaesthetic and analgesic effects have been suggested to be mediated by different

mechanisms. It has very high margin of safety, no irritation of the veins and no negative influence on ventilation or circulation. Its main disadvantages are that it produces hypertension and precipitates psychomimetic emergence phenomena.⁵ Fentanyl on other hand is the most frequently used opioid in clinical anaesthesia today. Its disadvantage is its negative influence on ventilation and postoperative nausea and vomiting. One of the main drawbacks with Ketamine anaesthesia has been emergence delirium, which Propofol seems to be effective in eliminating.^{6,7} In this study, the combination of Propofol- Ketamine was compared to the combination Propofol- Fentanyl in patients undergoing general anaesthesia for short elective surgeries. Haemodynamic variables, the time to recovery and patient acceptability were compared.

2. Materials and Methods

After obtaining approval from ethics committee and well informed written consent, a double-blind study which is randomised (All the drugs were administered by a person not involved in the study) was conducted on 60 patients (as per convenience and sample size was not calculated) of ASA grade I and II (18 to 60 years) of either sex, scheduled for short surgical procedures including suction and evacuation, dilatation and curettage, debridement, close reduction in orthopaedics, skin grafting, incision and drainage of abscess, cyst removal, fibroadenoma excision. Patients were divided into 2 groups PK (n = 30) and PF (n = 30) as per convenience.

All patients underwent minimum investigation as required in individual cases viz. haemogram, blood sugar, LFT, RFT, SE, Viral Markers, urine for routine and microscopic examination, ECG, x-ray chest if needed. All patients were

kept nil orally for 8 hours before scheduled surgery and written informed consents were taken. All patients were premedicated with injection glycopyrrolate 10mcg/kg body weight intravenously (IV) and injection Ondansetron. Upon arrival of the patient in the operation room, intravenous access with one 18 G cannula was established. 500 mL of crystalloid (Ringer lactate) solution started from one intravenous cannula. Electrocardiogram (ECG) leads placed, noninvasive arterial blood pressure (NIBP), pulse oximetry monitored. All baseline vital parameters, heart rate, respiratory rate, blood pressure, oxygen saturation (SPO₂) were monitored. All the drugs, ketamine, propofol and fentanyl were administered by a person not involved in the study to avoid bias. Drugs were given by intravenous route (I/V) for induction of anaesthesia and by infusion pump for maintenance of anaesthesia. Group PK (n = 30) received propofol 2.5 mg/kg + Ketamine 1 mg/kg for induction and propofol 2 mg/kg/hr. + ketamine 0.5 mg/kg/hr. for maintenance of anaesthesia. Group PF (n=50) received propofol 2.5 mg/kg + Fentanyl 1µg/kg for induction and propofol 2 mg/kg/hr. + Fentanyl 0.5µg/kg/hr. for maintenance of anaesthesia. All baseline haemodynamic parameters HR, SBP, DBP, SPO₂ were recorded before induction and immediately after induction, then every 5 minutes till 30 minutes, then every 10 minutes till the end of procedure and every 10 minutes till 30 minutes postoperatively. The incidence of postoperative nausea and vomiting (PONV) hallucinations, hypertension, hypotension, tachycardia, bradycardia, chest wall rigidity, nystagmus, myoclonic movements were monitored and were managed accordingly, recovery profile was assessed. Patient's satisfaction was assessed using a 100-mm visual analogue scale (VAS) (0 = least satisfied, 100 = most satisfied). Obtained data were tabulated and subjected to statistical analysis like student's t-test and chi-square test by SPSS-17 software. The p-value >0.05 was taken to be statistically insignificant and p-value.

3. Results

Demographic Data among both the groups were comparable for mean age, weight and sex ratio. P value (≥ 0.05) is nonsignificant. (Table no. 1). Values of pulse rate are shown as mean + SD. P value ≥ 0.05 , is not significant, there was no statistically significant change in pulse rate perioperatively (Table No. 2). Changes in systolic blood pressure (mmHg): Value are shown as mean \pm SD. At basal level, there was no significant difference statistically. There was statistically significant fall in systolic blood pressure after induction in Propofol - Fentanyl group. P value is 0.0001 is highly significant. After starting the infusion systolic blood pressure did not show any significant difference. (Table No.3). Changes diastolic blood pressure (mmHg): Value are shown as mean \pm SD. At basal level, there was no significant difference statistically. It was observed that mean diastolic blood pressure before induction were 77.88 ± 7.04 mmHg and 78.72 ± 3.87 mmHg in PK and PF group respectively. After induction DBP did not show any significant difference in both the groups. P value ≥ 0.05 is non-significant. (Table No.4). There is no statistically significant difference in SpO₂ (%) among both groups during various stages of surgical procedure. P value is ≥ 0.05 statistically insignificant.

Table 1: Demographic Profile

Variables	Group PK(N=30)	Group PF(N=30)	p value
Age	31.10 \pm 12.31	29.74 \pm 11.21	0.546
Weight	53.48 \pm 8.06	52.46 \pm 7.69	0.494
Sex(m/f)	16/34	18/32	0.079
ASA Grade I/II	10/40	05/45	0.090

Table 2: Comparison of change in pulse rate

Time	Group PK	Group PF	P Value
Before induction	79.02 \pm 3.10	77.96 \pm 3.14	0.089
Immediately after induction	81.24 \pm 4.03	80.52 \pm 2.13	0.237
5mins	83.10 \pm 5.34	82.32 \pm 2.59	0.360
10mins	84.40 \pm 4.86	83.80 \pm 5.16	0.561
15mins	84.98 \pm 4.41	83.68 \pm 2.78	0.088
20mins	84.48 \pm 4.17	83.24 \pm 2.64	0.082
25 mins	82.68 \pm 3.58	81.72 \pm 2.21	0.103
30 mins	79.24 \pm 2.76	78.52 \pm 2.27	0.121
After recovery (end of procedure)	76.48 \pm 3.06	77.22 \pm 2.29	0.213
10 mins after procedure	74.76 \pm 5.92	75.84 \pm 2.09	0.262
20 mins after procedure	74.04 \pm 6.12	74.28 \pm 1.80	0.799
30 mins after procedure	73.56 \pm 4.20	73.32 \pm 1.54	0.729

Table 3: Comparison of change in systolic BP

Time	Group PK	Group PF	P Value
Before induction	120.96 \pm 8.24	120.96 \pm 4.18	1.0
Immediate after induction	119.08 \pm 4.10	114.62 \pm 6.47	0.0001
5 mins after induction	119.48 \pm 4.27	118.22 \pm 2.82	0.128
10 mins	119.80 \pm 5.09	119.98 \pm 2.60	0.840
15 mins	119.16 \pm 5.01	118.44 \pm 3.05	0.412
20 mins	119.04 \pm 4.10	117.72 \pm 2.99	0.078
25 mins	119.28 \pm 3.30	118.28 \pm 2.28	0.085
30 mins	119.16 \pm 3.02	119.00 \pm 1.57	0.730
After recovery (end of procedure)	120.04 \pm 6.71	120.12 \pm 2.75	0.939
10 mins	120.62 \pm 4.00	118.80 \pm 5.51	0.102
20 mins	119.72 \pm 4.21	119.04 \pm 4.06	0.458
30 mins	118.80 \pm 4.42	119.14 \pm 4.37	0.725

Table 4: Comparison of change in diastolic BP

Time	Group PK	Group PF	P Value
Before induction	77.88 \pm 7.04	78.72 \pm 3.87	0.472
Immediate after induction	79.76 \pm 6.33	78.04 \pm 3.21	0.117
5 mins	78.24 \pm 5.84	77.20 \pm 2.88	0.241
10 mins	78.00 \pm 5.84	76.52 \pm 3.04	0.164
15 mins	77.40 \pm 5.81	75.28 \pm 5.96	0.093
20 mins	76.28 \pm 11.46	77.36 \pm 5.22	0.547
25 mins	78.88 \pm 4.50	77.76 \pm 4.23	0.222
30 mins	78.40 \pm 4.55	78.10 \pm 3.62	0.702
After recovery (end of procedure)	79.0 \pm 4.10	78.24 \pm 3.88	0.302
10 mins	79.24 \pm 4.03	78.48 \pm 2.69	0.263
20 mins	78.52 \pm 3.97	79.60 \pm 3.10	0.154
30 mins	78.60 \pm 3.79	79.48 \pm 3.17	0.232

4. Discussion

The findings of this study indicate that there was no statistically significant difference among both groups (PK and PF) regarding haemodynamic variability, recovery profile and side effects. R. Mahajan et al¹ also observed no significant haemodynamic changes among both groups. Similar results were obtained from other studies.^{5,8,9,10,11}

There was a decrease in mean SBP (119.08 ± 4.10) and

(114.62 ± 6.47) in PK and PF group respectively immediately after induction. Later (mean ± SD) SBP remained stable among both groups at 5, 10, 15, 20, 25 min. and at the end of procedure. On applying statistical test for intergroup comparison, the difference in SBP was highly significant immediately after induction in PK group compared to PF group (P=0.0001) because propofol and fentanyl had been given IV bolus. Propofol causes hypotension due to its vagotonic effect and fentanyl inhibits baroreceptor reflex. After starting infusion difference in SBP at different time interval was statistically insignificant (P≥0.05). Bajwa S.J.S. et al³ observed that ketamine-propofol provide better control of SBP as compared to propofol-fentanyl. There was significant fall in SBP in PF group after induction (P≤0.05) while there was mild increase in SBP in PK group which is statistically insignificant (P≥0.05). Their findings are well in accordance with our study. Similar results were obtained from other studies.^{1,5,8,9,10,12,13} Vallejo M. C. et al⁵ also observed no statistical significance in their study. Similar results were obtained from other studies.^{7,10,14}. There was no change in mean respiratory rate in both groups immediately after the induction. After starting the infusion no significant (P ≤0.05) changes have been observed in mean RR at 5, 10, 15, 20, 25 min. and at the end of procedure in PK and PF group respectively. On statistical testing for intergroup comparison, the difference in RR between both groups at different time interval was statistically insignificant (P≥0.05). R. Mahajan et al¹ also observed no statistically significant (P≥0.05) difference with respect to respiratory rate among both groups. Similar results were obtained from other studies.^{5,9,10,15}

5. Conclusion

Following Conclusions are drawn from the Present Study-

- Both ketamine and fentanyl in propofol infusion for short surgical procedures are equally safe and efficacious.
- Infusion of propofol-ketamine and propofol-fentanyl both provides stable haemodynamics and good recovery profile.
- Patient satisfaction is good among both the groups with no significant adverse effects.

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