A COMPARATIVE EVALUATION 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, hundred consenting patients undergoing short elective surgeries were divided into two groups of fifty each. Group PF received propofol 2 mg/kg + fentanyl 2 µg/kg for induction and propofol 4 mg/kg/hr. + fentanyl 1 µg/kg/hr. for maintenance of anaesthesia and group PK received propofol 2 mg/kg + ketamine 1 mg/kg for induction and propofol 4 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.

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BACKGROUND

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.

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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 syringe³ 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.

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 100 patients (as per convenience and sample size was not calculated) of ASA grade I and II (15 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 = 50) and PF (n = 50) as per convenience.

PK (n = 50)	Ketamine - propofol group
PF (n = 50)	Fentanyl - propofol group

All patients undergo for minimum investigation as required in individual cases viz. haemogram, blood sugar, blood urea, urine for routine and microscopic examination, ECG, x-ray chest if needed. All patients were kept nil orally for 8 hours before scheduled surgery. All patients were premedicated with injection glycopyrrolate 0.01 mg/kg body weight intramuscularly (IM) 30 minutes before shifting to Operation room (OR). Upon arrival of the patient in the operation room, intravenous access with two 20 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 = 50) received propofol 2 mg/kg + Ketamine 1 mg/kg for induction and propofol 4 mg/kg/hr. + ketamine 1 mg/kg/hr. for maintenance of anaesthesia. Group PF (n=50) received propofol 2 mg/kg + Fentanyl 2 µg/kg for induction and propofol 4 mg/kg/hr. + Fentanyl 1 µg/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). The patients rated their satisfaction by making a vertical mark on the 100-mm line. Only patients with score ≥ 75 were considered satisfied. The exact question was "Are you satisfied with your sedation?" The following questions were asked after 30 minutes of surgery.

- What is your name?
- Where do you live?
- What is date today?
- What is present time?
- Are you having pain?

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 <0.05 taken statistically significant.

RESULTS

Demographic Data among both the groups were comparable for mean age, weight and sex ratio. P value (≥ 0.05) is non-significant. (Table no. 1).

Values of pulse rate are shown as mean $\pm$ 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 (Graph 2).

Variables		Group PK (n=50)	Group PF (n=50)	P Value
Age(yrs.)		31.10 $\pm$ 12.31	29.74 $\pm$ 11.21	0.546
Weight(kg)		53.48 $\pm$ 8.06	52.46 $\pm$ 7.69	0.494
Sex(m/f)		16/34	18/32	0.079
ASA Grade	II/I	10/40	05/45	0.090

Table 1. Demographic Profile

Time		Group PK (n = 50)	Group PF (n = 50)	P value
Before induction		79.02 ± 3.10	77.96 ± 3.14	0.089
Immediate after induction		81.24 ± 4.03	80.52 ± 2.13	0.237
5 Minutes		83.10 ± 5.34	82.32 ± 2.59	0.360
10 Minutes		84.40 ± 4.86	83.80 ± 5.16	0.561
15 Minutes		84.98 ± 4.41	83.68 ± 2.78	0.088
20 Minutes		84.48 ± 4.17	83.24 ± 2.64	0.082
25 Minutes		82.68 ± 3.58	81.72 ± 2.21	0.103
30 Minutes		79.24 ± 2.76	78.52 ± 2.27	0.121
After Recovery	End of Procedure	76.48 ± 3.06	77.22 ± 2.29	0.213
	10 Min.	74.76 ± 5.92	75.84 ± 2.09	0.262
	20 Min.	74.04 ± 6.12	74.28 ± 1.80	0.799
	30 Min.	73.56 ± 4.20	73.32 ± 1.54	0.729
Table 2. Comparison of Change in Pulse Rate				

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Time	Group PK (n = 50)	Group PF (n = 50)	P value
Before induction	120.96 ± 8.24	120.96 ± 4.18	1.0
Immediate After Induction	119.08 ± 4.10	114.62 ± 6.47	0.0001*
5 Minutes	119.48 ± 4.27	118.22 ± 2.82	0.128
10 Minutes	119.80 ± 5.09	119.98 ± 2.60	0.840
15 Minutes	119.16 ± 5.01	118.44 ± 3.05	0.412
20 Minutes	119.04 ± 4.10	117.72 ± 2.99	0.078
25 Minutes	119.28 ± 3.30	118.28 ± 2.28	0.085
30 Minutes	119.16 ± 3.02	119.00 ± 1.57	0.730
After Recovery			
End of Procedure	120.04 ± 6.71	120.12 ± 2.75	0.939
10 Min.	120.62 ± 4.00	118.80 ± 5.51	0.102
20 Min.	119.72 ± 4.21	119.04 ± 4.06	0.458
30 Min.	118.80 ± 4.42	119.14 ± 4.37	0.725

Table 3. Comparison of Changes in SBP (mmHg)

Time	Group PK (n = 50)	Group PF (n = 50)	P Value
Before induction	77.88 ± 7.04	78.72 ± 3.87	0.472
Immediate after induction	79.76 ± 6.33	78.04 ± 3.21	0.117.
5 minutes	78.24 ± 5.84	77.20 ± 2.88	0.241
10 minutes	78.00 ± 5.84	76.52 ± 3.04	0.164
15 minutes	77.40 ± 5.81	75.28 ± 5.96	0.093
20 minutes	76.28 ± 11.46	77.36 ± 5.22	0.547
25 minutes	78.88 ± 4.50	77.76 ± 4.23	0.222
30 minutes	78.40 ± 4.55	78.10 ± 3.62	0.702
After recovery			
End of procedure	79.0 ± 4.10	78.24 ± 3.88	0.302
10 min.	79.24 ± 4.03	78.48 ± 2.69	0.263
20 min.	78.52 ± 3.97	79.60 ± 3.10	0.154
30 min.	78.60 ± 3.79	79.48 ± 3.17	0.232

Table 4. Comparison of Changes in DBP (mmHg)

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 ($P \leq 0.05$) 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 ($P \geq 0.05$). R. Mahajan et al¹ also observed no statistically significant ($P \geq 0.05$) difference with respect to respiratory rate among both groups. Similar results were obtained from other studies.^{5,9,10,15}

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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